Access DB# 92925

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Jennifer Maynard Examiner #: 76530 Date: [redacted] 01 May 2003
Art Unit: 3763 Phone Number 305-1356 Serial Number: 09/811754
Mail Box and Bldg/Room Location: CP2-3616 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Use of Streptomyces Hyaluronolyticus Enzyme in Opthalmic Treatments

Inventors (please provide full names): Christopher Ed Schuler

Earliest Priority Filing Date: 19 March 2001

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

terms: eye, ocular, cornea, vitreous humor, iris, Schlemm's canal, trabecular meshwork, trabeculum, retina, choroid

topical, injection, etc. applications to the eye

hyaluronidase and saline
↓
protease-free

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: JEANNE HORRIGAN	NA Sequence (#)		STN	✓
Searcher Phone #: 305-5934	AA Sequence (#)		Dialog	✓
Searcher Location: CP2-2C08	Structure (#)		Questel/Orbit	
Date Searcher Picked Up: 5/1	Bibliographic	✓	Dr.Link	
Date Completed: 5/1	Litigation		Lexis/Nexis	
Searcher Prep & Review Time: 100	Fulltext	✓	Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time: 50	Other		Other (specify)	

PTO-1590 (8-01) 5/1
12:40 - 4:20

BEST AVAILABLE COPY

May 1, 2003 ✓

TO: Jennifer Maynard, Art Unit 3763
CP2, Room 3-E-16

FROM: Jeanne Horrigan
ASRC Searcher in EIC3700

SUBJECT: Search Results for Serial 09/811754

Attached are the search results for the hyaluronidase and saline for the eye, including results of prior art searches in medical and general sci/tech and in foreign/international patent databases

The results are organized into two sets:

- Results of prior art search in foreign/international patent databases; and
- Results of non-patent literature search.

Results appear after the database names and search strategy used for those results. I tagged items that I thought seemed most relevant, but **I suggest that you review all of the results.**

Also attached is a search feedback form. Completion of the form is voluntary. Your completing this form would help us improve our search services.

I hope the attached information is useful. Please feel free to contact me (phone 305-5934 or email jeanne.horrigan@uspto.gov) if you have any questions or need additional searching on this application.

```
     (FILE 'HOME' ENTERED AT 12:59:18 ON 01 MAY 2003)
     FILE 'REGISTRY' ENTERED AT 12:59:26 ON 01 MAY 2003
               E HYALURONIDASE/CN
L1             4 S E3
               E HYALURONOGLUCOSAMINIDASE/CN
L2             1 S E3
L3             1 S SODIUM CHLORIDE/CN
               E SODIUM CHLORIDE/CN
L4             1 S E3
               E SALINE/CN
L5             1 S E3
               E PROTEASE/CN
L6             1 S E3
               E ENDOPEPTIDASE/CN
L7             1 S E3
     FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 13:00:52 ON 01 MAY 2003
L8         13024 S L1 OR L2
L9           370 S L5
L10        90128 S L6 OR L7
L11            2 S L8 AND L9
L12       955510 S EYE OR EYES OR OCUL? OR INTRAOCULAR OR CORNEA OR CORNEAL OR K
L13       467068 S VITREOUS OR VITREC? OR IRIS IR IRITIS OR SCHLEMM?(2A)CANAL OR
L14       194165 S L3 OR L9
L15          151 S L8 AND L14
L16      1236166 S L12 OR L13
L17            6 S L15 AND L16
L18            6 DUPLICATE REMOVE L17 (0 DUPLICATES REMOVED)

L18  ANSWER 1 OF 6  EMBASE  COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER:   2002411154  EMBASE
TITLE:              6(th) Yahya Cohen lecture: Visual experience during
                    cataract surgery.
AUTHOR:             Au Eong K.G.
CORPORATE SOURCE:   Dr. K.G. Au Eong, Eye Institute, National Healthcare Group,
                    Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore
                    308433, Singapore. Kah_Guan_Au_Eong@ttsh.com.sg
SOURCE:             Annals of the Academy of Medicine Singapore, (2002) 31/5
                    (666-674).
                    Refs: 36
                    ISSN: 0304-4602  CODEN: AAMSCG
COUNTRY:            Singapore
DOCUMENT TYPE:      Journal; Conference Article
FILE SEGMENT:       012     Ophthalmology
                    024     Anesthesiology
                    037     Drug Literature Index
                    038     Adverse Reactions Titles
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB   Introduction: The visual sensations many patients experience during
     cataract surgery under local anaesthesia have received little attention
     until recently. This paper reviews the recent studies on this phenomenon,
     discusses its clinical significance and suggests novel approaches to
     reduce its negative impact on the surgery. Methods: Literature review.
     Results: Many patients who have cataract surgery under retrobulbar,
     peribulbar or topical anaesthesia experience a variety of visual
     sensations in their operated   ***eye***   during surgery. These visual
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sensations include perception of light, movements, flashes, one or more colours, surgical instruments, the surgeon's hand/fingers, the surgeon and changes in light brightness. Some patients experience transient no light perception, even if the operation is performed under topical anaesthesia. The clinical significance of this phenomenon lies in the fact that approximately 7.1% to 15.4% of patients find their visual experience frightening. This fear and anxiety may cause some patients to become uncooperative during surgery and trigger a sympathetic surge, causing such undesirable effects as hypertension, tachycardia, ischaemic strain on the heart, hyperventilation and acute panic attack. Several approaches to reduce the negative impact of patients' visual experience are suggested, including appropriate preoperative counselling and reducing the ability of patients to see during surgery. Conclusions: The findings that some patients find their intraoperative visual experience distressing have a major impact on the way ophthalmologists manage their cataract patients. To reduce its negative impact, surgeons should consider incorporating appropriate preoperative counselling on potential intraoperative visual experience when obtaining informed consent for surgery.

CT Medical Descriptors:
*cataract extraction
*visual disorder: SI, side effect
eye surgery
experience
anesthesiological techniques
brightness
visual impairment: SI, side effect
surgical instrument
patient compliance
hypertension: CO, complication
tachycardia: CO, complication
heart muscle ischemia: CO, complication
preoperative care
preoperative evaluation
patient counseling
intraoperative period
analgesia
drug effect
akinesia
anophthalmia
phacoemulsification
surgical risk
risk assessment
pupil disease: SI, side effect
evoked visual response
drug induced disease: SI, side effect
human
clinical trial
conference paper
Drug Descriptors:
anesthetic agent: AE, adverse drug reaction
anesthetic agent: CT, clinical trial
anesthetic agent: AD, drug administration
anesthetic agent: CB, drug combination
anesthetic agent: CL, intracameral drug administration
anesthetic agent: RP, regional perfusion
anesthetic agent: RB, retrobulbar drug administration

anesthetic agent: TP, topical drug administration
lidocaine: AE, adverse drug reaction
lidocaine: CT, clinical trial
lidocaine: CB, drug combination
lidocaine: CL, intracameral drug administration
adrenalin
hyaluronidase
sedative agent: AE, adverse drug reaction
sedative agent: AD, drug administration
sedative agent: IV, intravenous drug administration
sedative agent: PO, oral drug administration
anxiolytic agent: AE, adverse drug reaction
anxiolytic agent: AD, drug administration
anxiolytic agent: IV, intravenous drug administration
anxiolytic agent: PO, oral drug administration
sodium chloride: CT, clinical trial
sodium chloride: CB, drug combination
sodium chloride: CL, intracameral drug administration
RN (lidocaine) 137-58-6, 24847-67-4, 56934-02-2, 73-78-9; (adrenalin) 51-43-4, 55-31-2, 6912-68-1; (hyaluronidase) ***9001-54-1*** , 9055-18-9; (sodium chloride) ***7647-14-5***

L18 ANSWER 2 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002345171 EMBASE
TITLE: Multilayered amniotic membrane transplantation for partial thickness scleral thinning following pterygium surgery [2].
AUTHOR: Sridhar M.S.; Bansal A.K.; Rao G.N.
CORPORATE SOURCE: M.S. Sridhar, Cornea Service, LV Prasad Eye Institute, LV Prasad Marg, Hyderabad 500 034, India. mss@lvpeye.stph.net
SOURCE: Eye, (2002) 16/5 (639-642).
Refs: 7
ISSN: 0950-222X CODEN: EYEEEC
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
LANGUAGE: English
CT Medical Descriptors:
*amnion
*transplantation
*sclera disease: CO, complication
*sclera disease: DT, drug therapy
*sclera disease: SU, surgery
pterygium: SU, surgery
pain: DI, diagnosis
eye disease
visual system examination
visual acuity
cornea disease: CO, complication
cornea disease: DI, diagnosis
cornea disease: DT, drug therapy
peribulbar anesthesia
surgical technique
suturing method
conjunctiva
phacoemulsification

epithelization
human
female
case report
controlled study
adult
letter
Drug Descriptors:
gentamicin: DT, drug therapy
artificial tear: DT, drug therapy
lidocaine: CB, drug combination
adrenalin: CB, drug combination
bupivacaine: CB, drug combination
hyaluronidase
sodium chloride
penicillin G
streptomycin
neomycin
amphotericin B
prednisolone acetate: DT, drug therapy
prednisolone acetate: TP, topical drug administration
ciprofloxacin: DT, drug therapy
betamethasone sodium phosphate: DT, drug therapy
steroid: DT, drug therapy
steroid: TP, topical drug administration
RN (gentamicin) 1392-48-9, 1403-66-3, 1405-41-0; (lidocaine) 137-58-6, 24847-67-4, 56934-02-2, 73-78-9; (adrenalin) 51-43-4, 55-31-2, 6912-68-1; (bupivacaine) 18010-40-7, 2180-92-9, 55750-21-5; (hyaluronidase) ***9001-54-1*** , 9055-18-9; (sodium chloride) ***7647-14-5*** ; (penicillin G) 1406-05-9, 61-33-6; (streptomycin) 57-92-1; (neomycin) 11004-65-2, 1404-04-2, 1405-10-3, 8026-22-0; (amphotericin B) 1397-89-3, 30652-87-0; (prednisolone acetate) 52-21-1, 52628-64-5; (ciprofloxacin) 85721-33-1; (betamethasone sodium phosphate) 151-73-5, 360-63-4

L18 ANSWER 3 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002187135 EMBASE
TITLE: Effect of alkalinization and/or hyaluronidase adjuvancy on a local anesthetic mixture for sub-Tenon's ophthalmic block.
AUTHOR: Moharib M.M.; Mitra S.; Rizvi S.G.
CORPORATE SOURCE: Dr. M.M. Moharib, Dept. Of Anesthesia/ICU, Sultan Qaboos University Hospital, PO Box 38, Muscat 123, Oman. magdi@omantel.net.om
SOURCE: Acta Anaesthesiologica Scandinavica, (2002) 46/5 (599-602). Refs: 19
ISSN: 0001-5172 CODEN: AANEAB
COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background and objectives: pH adjustment and/or addition of hyaluronidase to local anesthetic drugs decrease the time to onset and prolong the

duration of regional anesthetic techniques for ***ocular*** surgery. The objective of this study was to investigate whether these factors are effective also in sub-Tenon's block. Methods: Sixty patients were randomly assigned to four groups in a double blind, prospective fashion, and received 5.125ml mixtures as follows: 2.5ml lignocaine 2%, 2.5ml bupivacaine 0.5% and 0.125ml isotonic saline (group LB); 2.5ml lignocaine 2%, 2.5ml bupivacaine 0.5%, 15IU hyaluronidase/ml and 0.125 ml isotonic saline (group LBH); 2.5ml lignocaine 2%, 2.5ml bupivacaine 0.5% and 0.125ml sodium bicarbonate 8.4% (group LBpH); and 2.5ml lignocaine 2%, 2.5ml bupivacaine 0.5%, 15IU hyaluronidase/ml and 0.125 ml sodium bicarbonate 8.4% (group LBHpH). This measurement was based on one quadrant sub-Tenon's block. Akinesia was assessed every 30 s. Results: No statistically significant differences were found between the groups regarding mean times to onset and to complete akinesia. Group LBH displayed a significantly lower frequency of patients experiencing pain and a lower need for rescue medication during surgery than the other groups. Conclusion: pH adjustment and/or addition of hyaluronidase to a mixture of lignocaine and bupivacaine did not shorten the time to onset of akinesia following sub-Tenon's technique. However, the addition of hyaluronidase was associated with a lower fraction of patients experiencing pain during surgery. .COPYRGT. Acta Anaesthesiologica Scandinavica 46 (2002).

CT Medical Descriptors:
*alkalinization
****eye surgery***
*local anesthesia
pH
akinesia
technique
analgesia
functional anatomy
drug effect
titrimetry
intermethod comparison
treatment outcome
human
male
female
major clinical study
clinical trial
randomized controlled trial
controlled study
aged
adult
article
priority journal
Drug Descriptors:
*hyaluronidase: CT, clinical trial
*hyaluronidase: AD, drug administration
*hyaluronidase: CM, drug comparison
lidocaine: CT, clinical trial
lidocaine: AD, drug administration
lidocaine: CM, drug comparison
bupivacaine: CT, clinical trial
bupivacaine: AD, drug administration
bupivacaine: CM, drug comparison

sodium chloride: AD, drug administration
RN (hyaluronidase) ***9001-54-1*** , 9055-18-9; (lidocaine) 137-58-6, 24847-67-4, 56934-02-2, 73-78-9; (bupivacaine) 18010-40-7, 2180-92-9, 55750-21-5; (sodium chloride) ***7647-14-5***
CN (1) Xylocaine; (2) Marcaine; (3) Hyalase
CO (2) Astra (Sweden); (3) CP Pharmaceuticals (United Kingdom)

L18 ANSWER 4 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002059019 EMBASE
TITLE: ***Corneal*** toxicity of ***intraocular*** hyaluronidase.
AUTHOR: Jumper J.M.; McCauley M.B.; Equi R.A.; Duncan K.G.; Duncan J.; Schwartz D.M.
CORPORATE SOURCE: Dr. J.M. Jumper, 59 MDW/MCST, 2200 Bergquist Dr., Lackland AFB, TX 78236-5300, United States. mikejumper@yahoo.com
SOURCE: Journal of Ocular Pharmacology and Therapeutics, (2002) 18/1 (89-97).
Refs: 26
ISSN: 1080-7683 CODEN: JOPTFU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 012 Ophthalmology
037 Drug Literature Index
039 Pharmacy
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The purpose of this study was to examine the ***corneal*** toxicity of different preparations of ***intraocular*** hyaluronidase. SDS-PAGE analysis of bovine testicular hyaluronidase (Wydase.RTM.) and chromatographically purified hyaluronidase (Sigma.RTM.) was performed. These two preparations were injected into the anterior chamber of rabbits in amounts ranging from 1.5-150 IU (Wydase.RTM.) and 1.5-300 IU (Sigma.RTM.). A third set of rabbit ***eyes*** received Wydase.RTM. vehicle alone or in combination with Sigma.RTM. hyaluronidase. Treated control ***eyes*** were injected with saline. Slit lamp examination and indirect ophthalmoscopy were performed preoperatively and on postoperative days 1 and 7. Light microscopy of the corneas was performed. SDS-PAGE of Wydase.RTM. revealed numerous protein impurities, while Sigma.RTM. demonstrated one protein band consistent with mammalian hyaluronidase. Persistent ***corneal*** edema, severe anterior chamber fibrin, and endothelial necrosis, were seen in the majority of ***eyes*** injected with Wydase.RTM. in amounts of 50 IU and greater (n = 11). Thirty percent (30%) of the ***eyes*** injected with the Sigma.RTM. preparation (n = 11) had localized ***corneal*** opacity similar to 50% of ***eyes*** injected with saline (n = 2). Of the rabbit ***eyes*** injected with the Wydase.RTM. vehicle (n = 19), 68% had toxic changes. Intracameral injection of Wydase.RTM. is toxic to the rabbit ***cornea*** in amounts of 50 IU and greater. A chromatographically purified preparation showed only transient local toxicity. Toxicity of Wydase.RTM. may be due to protein impurities and the thimerosal-containing vehicle.
CT Medical Descriptors:
****cornea injury: DI, diagnosis***
rabbit
drug impurity

dose response
drug formulation
polyacrylamide gel electrophoresis
anterior eye chamber
slit lamp
ophthalmoscopy
microscopy
cornea edema: DI, diagnosis
fibrin formation
necrosis: DI, diagnosis
cornea endothelium
cornea opacity: DI, diagnosis
nonhuman
animal experiment
controlled study
animal tissue
article
Drug Descriptors:
*hyaluronidase: DO, drug dose
*hyaluronidase: TO, drug toxicity
*hyaluronidase: PR, pharmaceutics
*hyaluronidase: CL, intracameral drug administration
dodecyl sulfate sodium
polyacrylamide gel
drug vehicle
sodium chloride
protein
fibrin: EC, endogenous compound
thiomersal
h 3631
RN (hyaluronidase) ***9001-54-1*** , 9055-18-9; (dodecyl sulfate sodium) 151-21-3; (sodium chloride) ***7647-14-5*** ; (protein) 67254-75-5; (fibrin) 9001-31-4; (thiomersal) 54-64-8
CN (1) Wydase; (2) H 3631
CO (1) Wyeth Ayerst (United States); (2) Sigma (United States)

L18 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:287559 BIOSIS
DOCUMENT NUMBER: PREV200100287559
TITLE: Induction of proliferative vitreoretinopathy-like lesions in mice.
AUTHOR(S): Gallo, J. E. (1); Canto Soler, M. V. (1); Dodds, R. A. (1); Hokfelt, T.; Villar, M. J. (1); Suburo, A. M. (1)
CORPORATE SOURCE: (1) Centro Academico de Salud, Universidad Austral, Pilar, Buenos Aires, B1629AHJ Argentina
SOURCE: IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S432. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology Fort Lauderdale, Florida, USA April 29-May 04, 2001
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
CC Biochemical Studies - General *10060
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Biochemical Studies - Proteins, Peptides and Amino Acids *10064

Enzymes - General and Comparative Studies; Coenzymes *10802
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies *15002
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Endocrine System - Neuroendocrinology *17020
Sense Organs, Associated Structures and Functions - Physiology and Biochemistry *20004
Sense Organs, Associated Structures and Functions - Pathology *20006
BC Muridae 86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Sense Organs (Sensory Reception)
IT Parts, Structures, & Systems of Organisms
epiretinal membrane: sensory system; ***eye*** : sensory system; iris: dilatation, sensory system; ***ocular*** fundus: sensory system; platelet-rich-plasma: blood and lymphatics, dose; ***retina*** : sensory system; subretinal membrane: sensory system; ***vitreous*** chamber: sensory system
IT Diseases
proliferative vitreoretinopathy-like lesion: ***eye*** disease, induction
IT Chemicals & Biochemicals
dispase: dose; glial fibrillary acidic protein [GFAP]: expression; hyaluronidase: dose; neuropeptide Y: Y1 receptor, expression; saline: dose
IT Miscellaneous Descriptors
vitreoretinal reaction; Meeting Abstract
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
mouse (Muridae): C3H.HeN, C57BL/6J, animal model, male
ORGN Organism Superterms
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
RN 42613-33-2 (DISPASE)
9001-54-1Q (HYALURONIDASE)
37259-53-3Q (HYALURONIDASE)
37288-34-9Q (HYALURONIDASE)
37326-33-3Q (HYALURONIDASE)
82785-45-3 (NEUROPEPTIDE Y)
31661-12-8 (SALINE)

L18 ANSWER 6 OF 6 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94276974 EMBASE
DOCUMENT NUMBER: 1994276974
TITLE: Glycosaminoglycan and collagen fibrillar interactions in the mouse ***corneal*** stroma.
AUTHOR: Nakamura M.; Kobayashi M.; Hirana K.; Kobayashi K.; Hoshino T.; Awaya S.
CORPORATE SOURCE: Department of Ophthalmology, Nagoya University School of Medicine, 65 Tsuruma-cho,Showa-ku, Nagoya 466, Japan
SOURCE: Matrix Biology, (1994) 14/4 (283-286).
ISSN: 0945-053X CODEN: MTBOEC
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English

SUMMARY LANGUAGE: English

AB When sections of mouse ***corneal*** stroma were treated with 20 mM adenosine 5'-triphosphate (ATP) in phosphate buffered saline, pH4.0, at 37.degree.C and observed by electron microscopy, numerous periodic fibrils with about 100-nm periodicity appeared which were the aggregated form of type VI collagen (type VI collagen fibrils). They occurred in close association with D-periodic fibrillar collagens (striated collagen fibrils).However, when the tissue was digested with chondroitinase ABC or testicular hyaluronidase prior to the ATP treatment, type VI collagen fibrils were segregated from striated collagen fibrils, even though the type VI collagen fibrils themselves aggregated to form the 100nm-periodic structures. ***Keratanase*** or Streptomyces hyaluronidase had no such effect. One possible suggestion is that the ATP-aggregated type VI collagen fibrils are connected with striated collagen fibrils through chondroitin/dermatan sulfate glycosaminoglycans.

CT Medical Descriptors:
****cornea stroma***
animal tissue
article
controlled study
electron microscopy
female
molecular interaction
mouse
nonhuman
periodicity
priority journal
streptomyces
Drug Descriptors:
*collagen fibril
collagen type 6
*glycosaminoglycan: EC, endogenous compound
adenosine triphosphate
chondroitin: EC, endogenous compound
chondroitin abc lyase
dermatan sulfate: EC, endogenous compound
hyaluronidase
phosphate
sodium chloride

RN (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (chondroitin) 9007-27-6; (chondroitin abc lyase) 9024-13-9; (dermatan sulfate) 24967-94-0; (hyaluronidase) ***9001-54-1*** , 9055-18-9; (phosphate) 14066-19-4, 14265-44-2; (sodium chloride) ***7647-14-5***

File 155:MEDLINE(R) 1966-2003/Apr W4

Set	Items	Description
S1	150548	'EYE'
S2	156645	OCUL? OR OPHTHALM? OR INTRAOCULAR
S3	31429	'CORNEA'
S4	109918	KERAT? OR CORNEAL OR VITREOUS OR VITRE?
S5	13396	'IRIS'
S6	29414	SCHLEMM?(2N)CANAL OR TRABECUL? OR CILIARY
S7	53270	'RETINA'
S8	370081	S1:S7
S9	5565	HYALURONIDASE OR HYALURONOGLUCOSAMINIDASE
S10	104626	SALINE OR SODIUM()CHLORIDE
S11	853075	TOPICAL? OR INJECT? OR SURFACE? ?
S12	81163	PROTEASE OR ENDOPEPTIDASE? ?
S13	7	S8 AND S9 AND S10 AND S11
S14	1	S13/2002:2003
S15	**6**	**S13 NOT S14**
S16	23	S8 AND S9 AND S10
S17	16	S16 NOT S13
S18	2	S17/2002:2003
S19	**14**	**S17 NOT S18**

15/6/2

11372169 98253080 PMID: 9590855

[An experimental study on compound anisodine III for softening scar of mouse skin after burn]

May 1996

15/6/4

07335022 92198110 PMID: 1550406

Methylprednisolone acetate induced release of cartilage proteoglycans: determination by high performance liquid chromatography.

Feb 1992

15/9/1

DIALOG(R)File 155:MEDLINE(R)

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11527407 98418455 PMID: 9747683

Efficacy of hyaluronidase **in reducing increases in** intraocular **pressure related to the use of viscoelastic substances.**

Harooni M; Freilich J M; Abelson M; Refojo M

Schepens Eye Research Institute, Harvard Medical School, Boston, Mass 02114, USA. sunyretina@aol.com

Archives of ophthalmology (UNITED STATES) Sep 1998, 116 (9) p1218-21 , ISSN 0003-9950 Journal Code: 7706534

Contract/Grant No.: EY00327; EY; NEI

Comment in Arch Ophthalmol. 2000 Mar;118(3) 445; Comment in PMID 10721981 ; Comment in Arch Ophthalmol. 2000 Mar;118(3):445-6; Comment in PMID 10721982

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

OBJECTIVE: To evaluate the efficacy of **hyaluronidase** in preventing increases in **intraocular** pressure related to **injections** of

hyaluronan-containing viscoelastic substances. METHODS: Twenty-five white rabbits were divided into 5 groups. In groups 1 through 4, 0.15 mL of aqueous humor was removed and replaced with 0.10 mL of a viscoelastic substance in both eyes. Additionally, 10 units of **hyaluronidase** (0.05 mL) was **injected** in the anterior chamber of the right **eye** , whereas the left **eye** was **injected** with a volumetrically equivalent dose of balanced **saline** solution. Viscoelastic substances tested were Healon and Healon GV (Pharmacia & Upjohn, Kalamazoo, Mich), Viscoat (Alcon Laboratories, Fort Worth, Tex), and Ocucoat (Storz **Ophthalmics** , Clearwater, Fla). In group 5, right eyes were **injected** with 10 units of **hyaluronidase** and the left eyes were treated with balanced **saline** solution. Results: After **injections** of viscoelastic substance, **intraocular** pressure rose rapidly, reaching a peak at approximately 46 hours after **injection** and returning to preinjection levels within 24 hours. **Hyaluronidase** significantly decreased **intraocular** pressure when used with Healon, Healon GV, and Viscoat, but not with Ocucoat. When **injected** in the absence of viscoelastic, **hyaluronidase** appeared to decrease **intraocular** pressure, but this result was not statistically significant. Conclusions: **Injections** of **hyaluronidase** into the anterior chamber of rabbits effectively prevent increases in **intraocular** pressure induced by hyaluronan-containing viscoelastic substances. This effect may be related to the ability of **hyaluronidase** to cleave hyaluronan moieties.

Tags: Animal; Comparative Study; Support, U.S. Gov't, P.H.S.

Descriptors: Chondroitin--adverse effects--AE; *Hyaluronic Acid--adverse effects--AE; * **Hyaluronoglucosaminidase** --administration and dosage--AD; * **Intraocular** Pressure--drug effects--DE; * **Ocular** Hypertension --prevention and control--PC; Anterior Chamber--drug effects--DE; Drug Combinations; **Injections** ; **Ocular Hypertension** --chemically induced--CI; **Ophthalmic** Solutions; Rabbits

CAS Registry No.: 0 (Drug Combinations); 0 (Ophthalmic Solutions); 123352-36-3 (Viscoat); 9004-61-9 (Hyaluronic Acid); 9007-27-6 (Chondroitin)

Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**)

Record Date Created: 19980928

Record Date Completed: 19980928

15/9/3

DIALOG(R)File 155:MEDLINE(R)

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08022067 94087791 PMID: 7505341

Effect of hyaluronidase **on brain extracellular matrix in vivo and optic nerve regeneration.**

Tona A; Bignami A

Department of Veterans Affairs Medical Center, West Roxbury, Massachusetts 02132.

Journal of neuroscience research (UNITED STATES) Oct 1 1993, 36 (2) p191-9, ISSN 0360-4012 Journal Code: 7600111

Contract/Grant No.: NS 13034; NS; NINDS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

In the rat, intracerebral **injection** of bacterial **hyaluronidase** resulted in the almost complete disappearance of hyaluronic acid (HA) and glial hyaluronate-binding protein (GHAP) from cerebral hemispheres, brain

stem, and cerebellum (but not from optic nerves and chiasm) starting 2-3 hr after the **injection** . HA and GHAP reappeared throughout the brain in characteristic patches 2-3 days after the 1injection . The patches gradually became confluent and after 12 days the brain appeared virtually normal. In normal rat optic nerve, staining for HA and GHAP ceased abruptly in the region of the lamina cribrosa. The **retina** was completely negative. HA and GHAP disappeared from **hyaluronidase - injected** optic nerve, chiasm, and contralateral optic nerve. In **hyaluronidase - injected** crushed optic nerves, regenerated axons were able to grow for short distances (about 500 microns) into the distal stump undergoing Wallerian degeneration. No such growth was observed in **saline - injected** controls.

Tags: Animal; Female; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: Brain--drug effects--DE; *Extracellular Matrix--drug effects --DE; * **Hyaluronoglucosaminidase** --pharmacology--PD; *Nerve Regeneration --drug effects--DE; *Optic Nerve--drug effects--DE; Antigens, CD44; Axons --physiology--PH; Brain--cytology--CY; Brain Chemistry--drug effects--DE; Carrier Proteins--biosynthesis--BI; Glial Fibrillary Acidic Protein --immunology--IM; Glial Fibrillary Acidic Protein--metabolism--ME; Hyaluronic Acid--metabolism--ME; Nerve Crush; Neurofilament Proteins --immunology--IM; Neurofilament Proteins--metabolism--ME; Optic Nerve --cytology--CY; Rats; Rats, Sprague-Dawley; Receptors, Cell **Surface** --biosynthesis--BI; Receptors, Lymphocyte Homing--biosynthesis--BI

CAS Registry No.: 0 (Antigens, CD44); 0 (Carrier Proteins); 0 (Glial Fibrillary Acidic Protein); 0 (Neurofilament Proteins); 0 (Receptors, Cell Surface); 0 (Receptors, Lymphocyte Homing); 9004-61-9 (Hyaluronic Acid)

Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**)

Record Date Created: 19940121

Record Date Completed: 19940121

15/9/5

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

06815997 91055938 PMID: 2242999

The safety of intravitreal hyaluronidase . A clinical and histologic study.

Gottlieb J L; Antoszyk A N; Hatchell D L; Saloupis P

Department of Ophthalmology, Duke University Eye Center, Durham, North Carolina 27710.

Investigative ophthalmology & visual science (UNITED STATES) Nov 1990, 31 (11) p2345-52, ISSN 0146-0404 Journal Code: 7703701

Contract/Grant No.: EY 02903; EY; NEI; EY 05722; EY; NEI; EY 06057-01; EY ; NEI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The authors previously developed a new model of preretinal neovascularization in the rabbit **eye** using **hyaluronidase** for enzymatic **vitreolysis** . The purpose of this study was to evaluate the safety of intravitreal **injections** of **hyaluronidase** . Concentrations of 1, 15, 30, 50, and 150 IU of **hyaluronidase** in 0.1 ml of 0.9% **saline** were **injected** intravitreally and aspirated repetitively until the **vitreous** was partially liquified. The animals were examined with indirect **ophthalmoscopy** , fundus photography, and fluorescein angiography before

injection and on days 1 and 7 after **injection** . Light and electron microscopic retinal sections were prepared from enucleated eyes at days 1 and 7. All concentrations of **hyaluronidase** were effective in producing partial **vitreolysis** . Eyes treated with 1 IU showed no abnormalities on days 1 or 7. Eyes treated with 15 IU showed no retinal abnormalities on day 1, but on day 7 histologic abnormalities were present in two of four eyes. At higher concentrations, clinical and histologic changes were seen in proportion to the concentration and included focal whitening, edema, **vitreous** haze, vascular abnormalities, and retinal necrosis at the highest doses. Histologic evaluation of the **retina** revealed marked destruction in all layers at the higher concentrations. The authors conclude that 1 IU of intravitreal **hyaluronidase** is sufficient for partial **vitreolysis** and nontoxic to the rabbit **retina** .

Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: **Hyaluronoglucosaminidase** --toxicity--TO; * **Retina** --drug effects--DE; * **Vitreous** Body--drug effects--DE; Drainage; Fluorescein Angiography; Fundus **Oculi** ; **Hyaluronoglucosaminidase** --administration and dosage--AD; **Ophthalmoscopy** ; Rabbits; **Retina** --pathology--PA; **Retina** --ultrastructure--UL

Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**)

Record Date Created: 19901231

Record Date Completed: 19901231

15/9/6

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
01521823 73171271 PMID: 4660311

Hyaluronic acid of vitreous **body in different pathologic states.**

Goswammy S; Cardoza A A; Mathur R L; Agarwal L P

Indian journal of medical research (INDIA) Jun 1972, 60 (6) p953-65, ISSN 0971-5916 Journal Code: 0374701

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Tags: Animal

Descriptors: Ascorbic Acid--analysis--AN; * **Eye** Diseases--metabolism--ME ; *Hexosamines--analysis--AN; * **Vitreous** Body--analysis--AN; Blood; Chromatography; **Eye** Diseases--enzymology--EN; **Hyaluronoglucosaminidase** --analysis--AN; **Injections** ; Optics; Rabbits; **Sodium Chloride** ; Staphylococcal Infections--metabolism--ME; Viscosity; **Vitreous** Body --enzymology--EN

CAS Registry No.: 0 (Hexosamines); 50-81-7 (Ascorbic Acid); 7647-14-5 (Sodium Chloride)

Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**)

Record Date Created: 19730702

Record Date Completed: 19730702

19/9/3

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
09159967 20462762 PMID: 11009238

Alkalinized lidocaine and bupivacaine with hyaluronidase **for**

sub-tenon's ophthalmic **block.**
Moharib M M; Mitra S
Department of Anaesthesia/ICU, Sultan Qaboos University Hospital, Muscat, Oman. magdi@omantel.net.om
Regional anesthesia and pain medicine (UNITED STATES) Sep-Oct 2000, 25 (5) p514-7, ISSN 1098-7339 Journal Code: 9804508
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
BACKGROUND AND OBJECTIVES: Alkalinization of local anesthetics has been shown to decrease the onset and prolong the duration of block for extraconal and intraconal application in **ocular** surgery. The objective of this study is to determine if alkalinization is also effective in sub-Tenon's block when **hyaluronidase** is added to the drug mixture. METHODS: Twenty-nine patients were randomly assigned to 2 groups in a double-blind, prospective fashion to receive 5.125 mL of either a plain mixture LBH (2.5 mL lidocaine 2%, 2.5 mL bupivacaine 0.5%, 5 IU/mL **hyaluronidase** , and 0.125 mL isotonic **saline**) or pH-adjusted mixture LBH-PH (2.5 mL lidocaine 2%, 2.5 mL bupivacaine 0.5%, 5 IU/mL **hyaluronidase** , and 0.125 mL sodium bicarbonate 8.4%) of local anesthetics in a 1-quadrant sub-Tenon's block. Time to onset and time to full akinesia were determined every 30 seconds. RESULTS: No difference was found between the study groups. CONCLUSION: pH adjustment of the local anesthetic mixture of lidocaine, bupivacaine, and **hyaluronidase** offered no additional benefit in sub-Tenon's technique in **ocular** procedures.
Tags: Female; Human; Male
Descriptors: Bupivacaine--administration and dosage--AD; * **Hyaluronoglucosaminidase** --administration and dosage--AD; *Lidocaine --administration and dosage--AD; *Nerve Block; Adult; Aged; Double-Blind Method; Hydrogen-Ion Concentration; Middle Age; **Ophthalmologic** Surgical Procedures; Prospective Studies
CAS Registry No.: 137-58-6 (Lidocaine); 2180-92-9 (Bupivacaine)
Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**)
Record Date Created: 20010112
Record Date Completed: 20010112

19/9/4
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
08779321 20061163 PMID: 10595714
Pretreatment methods to improve nerve immunostaining in corneas from long-term fixed embryonic quail eyes.
Barrett J E; Wells D C; Conrad G W Conrad G W KS St U, Manhattan
Division of Biology, Kansas State University, Manhattan 66506-4901, USA.
Journal of neuroscience methods (NETHERLANDS) Oct 15 1999, 92 (1-2) p161-8, ISSN 0165-0270 Journal Code: 7905558
Contract/Grant No.: EY00952; EY; NEI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Pretreatment methods were used to improve neurofilament immunostaining in corneas from embryonic day 16 Japanese quail corneas that had been stored

in fixative solution for several months. A sequential combination of the following three pretreatments: brief microwave heating in **saline** , followed by extraction with sodium dodecyl sulfate (SDS) at 37 degrees C, followed by digestion with **hyaluronidase** at 37 degrees C, produced significantly increased antibody staining of **corneal** neurofilament proteins, compared with embryonic corneas subjected to no prior pretreatments or to single or two-step protocols. After applying the sequence of all three pretreatments, darkest nerve staining and increased numbers of fine branches were observed, together with lower background staining. Thus, the result of applying the three-step pretreatment sequence is better than that of applying any of its component single pretreatments or even combinations of any two of them. These findings therefore suggest that each of these three pretreatments causes a unique effect, beneficial to immunostaining of neurofilament proteins, and that their individual effects are independent and additive. In addition to embryonic corneas, the three-step procedure also may be useful for immunostaining of nerves in other very delicate, highly-hydrated tissues containing an abundance of extracellular matrix.

Tags: Animal; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: **Cornea** --chemistry--CH; *Formaldehyde; * **Hyaluronoglucosaminidase** ; *Immunohistochemistry--methods--MT; *Neurofilament Proteins--analysis--AN; *Polymers; *Sodium Dodecyl Sulfate; **Cornea** --embryology--EM; **Eye** --chemistry--CH; **Eye** --embryology--EM; Quail; **Sodium Chloride**

CAS Registry No.: 0 (Neurofilament Proteins); 0 (Polymers); 151-21-3 (Sodium Dodecyl Sulfate); 30525-89-4 (paraform); 50-00-0 (Formaldehyde); 7647-14-5 (Sodium Chloride)

Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**) Identifiers: *NASA Discipline Developmental Biology; *Non-NASA Center

Record Date Created: 20000104

Record Date Completed: 20000104

19/9/5

DIALOG(R)File 155:MEDLINE(R)

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08440413 95128517 PMID: 7827750

Glycosaminoglycan and collagen fibrillar interactions in the mouse corneal stroma.

Nakamura M; Kobayashi M; Hirano K; Kobayashi K; Hoshino T; Awaya S

Department of Ophthalmology, Nagoya University School of Medicine, Japan.

Matrix biology - journal of the International Society for Matrix Biology (GERMANY) Aug 1994, 14 (4) p283-6, ISSN 0945-053X Journal Code: 9432592

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

When sections of mouse **corneal** stroma were treated with 20 mM adenosine 5'-triphosphate (ATP) in phosphate buffered **saline** , pH 4.0, at 37 degrees C and observed by electron microscopy, numerous periodic fibrils with about 100-nm periodicity appeared which were the aggregated form of type VI collagen (type VI collagen fibrils). They occurred in close association with D-periodic fibrillar collagens (striated collagen fibrils). However, when the tissue was digested with chondroitinase ABC or testicular

hyaluronidase prior to the ATP treatment, type IV collagen fibrils were segregated from striated collagen fibrils, even though the type VI collagen fibrils themselves aggregated to form the 100 nm-periodic structures. **Keratanase** or Streptomyces **hyaluronidase** had no such effect. One possible suggestion is that the ATP-aggregated type VI collagen fibrils are connected with striated collagen fibrils through chondroitin/dermatan sulfate glycosaminoglycans.

Tags: Animal; Female

Descriptors: Collagen--metabolism--ME; * **Cornea** --metabolism--ME; *Glycosaminoglycans--metabolism--ME; Adenosine Triphosphate--pharmacology --PD; Chondroitin Lyases--pharmacology--PD; **Cornea** --drug effects--DE; **Cornea** --ultrastructure--UL; **Hyaluronoglucosaminidase** --pharmacology--PD; Mice; Microscopy, Electron; beta-Galactosidase--pharmacology--PD

CAS Registry No.: 0 (Glycosaminoglycans); 56-65-5 (Adenosine Triphosphate); 9007-34-5 (Collagen)

Enzyme No.: EC 3.2.1.103 (**keratan** -sulfate endo-1,4-beta-galactosidase); EC 3.2.1.23 (beta-Galactosidase); EC 3.2.1.35 (**Hyaluronoglucosaminidase**); EC 4.2.2.- (Chondroitin Lyases)

Record Date Created: 19950221

Record Date Completed: 19950221

19/9/6

DIALOG(R)File 155:MEDLINE(R)

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06247233 89263071 PMID: 2726146

The effect of hyaluronidase **on akinesia during cataract surgery.**

Abelson M B; Mandel E; Paradis A; George M

Eye Research Institute, Boston, Mass. 02114.

Ophthalmic surgery (UNITED STATES) May 1989, 20 (5) p325-6, ISSN 0022-023X Journal Code: 0241035

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The ability of **hyaluronidase** to improve akinesis in retrobulbar anesthesia was evaluated in a double-masked study. Forty consecutive patients undergoing cataract surgery were anesthetized with 3 ml of a 1:1 mixture of 4.0% lidocaine and 0.75% bupivacaine solution. In a predetermined randomized fashion, 2 ml of **hyaluronidase** (300 USP units) were added to half of the syringes, and 2 ml of **saline** to the remaining half. The level of akinesia was graded in six different positions of gaze. Seventy percent of the **hyaluronidase** group exhibited complete akinesis, while only 40% of the control group did. The mean scores for four out of six positions of gaze were significantly higher in the **hyaluronidase** patients than in the control group. Similarly, the **hyaluronidase** subjects showed a significantly higher sum score for the six sectors than did the control subjects ($p = .0001$). These results show that **hyaluronidase** significantly enhances akinesia. It is therefore recommended that it be included in the anesthetic regimen for such surgeries.

Tags: Comparative Study; Human; Support, Non-U.S. Gov't

Descriptors: Cataract Extraction; * **Eye** Movements--drug effects--DE; * **Hyaluronoglucosaminidase** --pharmacology--PD; Anesthesia, Local; Bupivacaine; Lidocaine

CAS Registry No.: 137-58-6 (Lidocaine); 2180-92-9 (Bupivacaine)

Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**)
Record Date Created: 19890707
Record Date Completed: 19890707

19/9/7
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
04367929 84009569 PMID: 6619739
Laser nephelometric determination of glycosaminoglycans--method and application.
Gressner A M; Scherer R; Stuhlsatz H W
Journal of clinical chemistry and clinical biochemistry. Zeitschrift fur klinische Chemie und klinische Biochemie (GERMANY, WEST) Jul 1983, 21 (7) p407-16, ISSN 0340-076X Journal Code: 7701860
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Light scattering due to the formation of insoluble complexes between the long-chain quaternary ammonium salt N-cetylpyridinium chloride and glycosaminoglycans was utilized for a relative simple, sensitive and precise determination of total and specific types of glycosaminoglycans by laser nephelometry. The addition of the ammonium salt to solutions of various glycosaminoglycans in 0.03 mol/l NaCl produces a time-dependent increase in light scattering, which reaches a maximum between 14 and 18 h of complex formation, irrespective of the type of glycosaminoglycan studied. Only **keratan** sulphate does not generate light scattering, and is therefore not detectable by the procedure. The scattering of laser light by certain types of sulphated glycosaminoglycans (e.g. heparan sulphate, heparin) depends more on the degree of sulphation (charge density) than on chain length within a certain range. Optimum light scattering was found at 28 mmol/l N-cetylpyridinium chloride and at a ionic strength around 0.03 mol/l NaCl. The detection limits and linear ranges of the individual glycosaminoglycans were evaluated. For the determination of chondroitin sulphate, laser nephelometry is at least 8 times more sensitive and much more simple than the modified carbazole method (glucuronic acid). The intra-assay and inter-assay coefficients of variation are about 4% and 7%, respectively. Laser nephelometry is much more sensitive than turbidimetry. Complex synthetic mixtures of glycosaminoglycans and biological fluids were accurately differentiated by successive chemical and enzymatic degradation of the respective glycosaminoglycans followed by the measurement of the resulting reduction of laser light scattering. In synovial fluids from non-inflammatory joint diseases, light scattering (units/ml) was about 4.5 times higher than in synovial fluids from inflammatory articular lesions. In both pathologic conditions nearly all of the light scattering can be attributed to hyaluronic acid.

Tags: Human
Descriptors: *Glycosaminoglycans--analysis--AN; *Lasers--diagnostic use --DU; Cetylpyridinium--diagnostic use--DU; Chondroitin Lyases--diagnostic use--DU; **Hyaluronoglucosaminidase** --diagnostic use--DU; Nephelometry and Turbidimetry--methods--MT; Nitrous Acid; Scattering, Radiation; **Sodium Chloride** ; Synovial Fluid--analysis--AN
CAS Registry No.: 0 (Glycosaminoglycans); 7647-14-5 (Sodium Chloride) ; 7773-52-6 (Cetylpyridinium); 7782-77-6 (Nitrous Acid)
Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**); EC 4.2.2.-

(Chondroitin Lyases)
Record Date Created: 19831123
Record Date Completed: 19831123

19/9/10

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
02681525 78108804 PMID: 146684
The canine eye: **in vitro dissolution of the barriers to aqueous outflow.**
Van Buskirk E M; Brett J
Investigative ophthalmology & visual science (UNITED STATES) Mar 1978, 17 (3) p258-71, ISSN 0146-0404 Journal Code: 7703701
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Facility of aqueous outflow and time-dependent changes in its **hyaluronidase** -sensitive and **hyaluronidase** -resistant components were evaluated in freshly excised canine eyes by constant pressure quantitative aqueous perfusion. Mean baseline facility of outflow was 0.24 microliter/min/mm Hg. With prolonged perfusion at constant **intraocular** pressure, facility of outflow was observed to increase almost linearly for at least 3 hr and continued to increase for up to 10 hr, reaching a maximum several times the initially measured facility. Perfusion with pooled dog aqueous humor did not prevent the time-dependent increase in measured facility. Rapid exchange of anterior chamber contents with perfusion solution alone produced an immediate threefold increase in facility, again followed by a gradual time-dependent facility increase. Rapid exchange of anterior chamber contents with **hyaluronidase** produced an immediate fivefold increase in facility with stabilization of measured facility over 3 hr and subsequent perfusion. The time-dependent changes in measured facility of outflow or "washout phenomenon" appeared to result from the gradual dissolution of the **hyaluronidase** -sensitive component of the barriers to aqueous outflow in the canine **eye** .
Tags: Animal; In Vitro; Support, U.S. Gov't, P.H.S.
Descriptors: *Aqueous Humor--physiology--PH; *Dogs--physiology--PH; Glycosaminoglycans--metabolism--ME; **Hyaluronoglucosaminidase** --pharmacology--PD; Perfusion; **Sodium Chloride** ; Time Factors
CAS Registry No.: 0 (Glycosaminoglycans); 7647-14-5 (Sodium Chloride)
Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**)
Record Date Created: 19780426
Record Date Completed: 19780426

19/9/11

DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
02301767 76265905 PMID: 134175
A comparative study of extracellular sulfated glycosaminoglycans synthesized by rabbit corneal **fibroblasts in organ and confluent cultures.**
Klintworth G K; Smith C F
Laboratory investigation; a journal of technical methods and pathology (UNITED STATES) Sep 1976, 35 (3) p258-63, ISSN 0023-6837 Journal Code: 0376617
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The extracellular sulfated glycosaminoglycans synthesized by explants of rabbit **cornea** and sclera, and by confluent cultures of **corneal** fibroblasts after incubation in medium containing 35S-sulfate were compared. The glycosaminoglycans isolated from **corneal** explants differed considerably from those obtained from confluent **corneal** fibroblast cultures and scleral explants. Only the **corneal** explants secreted into the nutrient medium a population of enzyme-resistant 35S-sulfate-labeled glycosaminoglycan that eluted from Dowex 1-X2 (Cl-) at a 3 M **sodium chloride** concentration, and which was resistant to testicular **hyaluronidase** , chondroitinase ABC, and nitrous acid degradation. With time, **corneal** explants gradually synthesized less of this fraction with these attributes of **keratosulfate** . If the **corneal** epithelium and endothelium remained on the **corneal** explants the total incorporated 35S-sulfate was approximately double that obtained when the **cornea** was striped of these cells.

Tags: Animal; Comparative Study; Support, U.S. Gov't, P.H.S.

Descriptors: Chondroitin--analogs and derivatives--AA; *Chondroitin Sulfates--biosynthesis--BI; * **Cornea** --metabolism--ME; *Glycosaminoglycans --biosynthesis--BI; * **Keratan** Sulfate--biosynthesis--BI; Cells, Cultured; **Cornea** --cytology--CY; Epithelial Cells; Epithelium--metabolism--ME; Extracellular Space--metabolism--ME; Fibroblasts--metabolism--ME; Rabbits; Sclera--cytology--CY; Sclera--metabolism--ME; Tissue Culture

CAS Registry No.: 0 (Glycosaminoglycans); 9007-27-6 (Chondroitin); 9007-28-7 (Chondroitin Sulfates); 9056-36-4 (Keratan Sulfate)

Record Date Created: 19761101
Record Date Completed: 19761101

19/9/13
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

02253159 76212527 PMID: 931693

Stromal sodium binding after glycosaminoglycan digestion.

Green K; Downs S; Bowman K

Investigative ophthalmology (UNITED STATES) Jun 1976, 15 (6) p484-6, ISSN 0020-9988 Journal Code: 0374730

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The glycosaminoglycans of isolated rabbit **corneal** stroma, clamped between two lucite plates at near normal hydration, were digested with testicular **hyaluronidase** in **saline** solution. After equilibration with 0.9 per cent **saline** solution alone the sodium and chloride content of the stroma was determined. Chloride was in equilibrium with both normal and **hyaluronidase** -treated stroma, allowing use of the Donnan calculation for excess or bound sodium to be made. Normal stromas contained 200 mEq. bound sodium per kilogram of dry weight calculated from the Donnan calculation; **hyaluronidase** -treated stromas contained 110 mEq. bound sodium per kilogram of dry weight. The data show that about half of the bound sodium in the **corneal** stroma is on nonsaccharide binding sites. Quantitative

verification of the loss of glycosaminoglycans was performed.
Tags: Animal; In Vitro; Support, U.S. Gov't, P.H.S.
Descriptors: **Cornea** --metabolism--ME; *Sodium--metabolism--ME; Binding Sites--drug effects--DE; Chlorine--analysis--AN; **Cornea** --analysis--AN; Glycosaminoglycans--analysis--AN; Glycosaminoglycans--metabolism--ME; **Hyaluronoglucosaminidase** --pharmacology--PD; Rabbits; Sodium--analysis--AN
CAS Registry No.: 0 (Glycosaminoglycans); 7440-23-5 (Sodium); 7782-50-5 (Chlorine)
Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**)
Record Date Created: 19760823
Record Date Completed: 19760823

19/9/14
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.
01986766 75162578 PMID: 165741
Electron microscopic studies on zonular fibers. II. Changes of the zonular fibers after the treatment with collagenase, alpha-chymotrypsin and hyaluronidase .
Takei Y; Smelser G K
Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie. Albrecht von Graefe's archive for clinical and experimental ophthalmology (GERMANY, WEST) 1975, 194 (3) p153-73, ISSN 0065-6100 Journal Code: 0044637
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Adult rabbit zonular fibers maintained in their native condition were treated with collagenase, alpha-chymotrypsin and **hyaluronidase** , and were observed with the electron microscope. The results obtained were as follows: 1. Collagenase digested the lens capsule, but not the zonular fibers. 2. Long time collagenase action obscured the cell membrane of the lens epithelium and the basal lamina of the **ciliary** epithelium. 3. Washing with 0.9% NaCl increased the collagenase action on the lens capsule. 4. Alpha-chymotrypsin digested the zonular fibers and the zonular lemalla, but not the lens capsule and the basal lamina of the **ciliary** epithelium. 5, **Hyaluronidase** only slightly changed the lens capsule. 6. The **vitreous** fibers were digested by collagenase, but not by alpha-chymotrypsin or **hyaluronidase** . Thes results together with the review of recent literature indicate that the zonular fiber has a nature close to that of the microfibril of elastic fiber.
Tags: Animal; Support, U.S. Gov't, P.H.S.
Descriptors: **Ciliary** Body--ultrastructure--UL; Chymotrypsin --pharmacology--PD; **Ciliary** Body--drug effects--DE; Connective Tissue --ultrastructure--UL; Elastic Tissue--ultrastructure--UL; **Hyaluronoglucosaminidase** --pharmacology--PD; Lens, Crystalline--drug effects--DE; Microbial Collagenase--pharmacology--PD; Rabbits; **Sodium Chloride** ; **Vitreous** Body--drug effects--DE
CAS Registry No.: 7647-14-5 (Sodium Chloride)
Enzyme No.: EC 3.2.1.35 (**Hyaluronoglucosaminidase**); EC 3.4.21.1 (Chymotrypsin); EC 3.4.24.3 (Microbial Collagenase)
Record Date Created: 19750728
Record Date Completed: 19750728

```
File   5:Biosis Previews(R) 1969-2003/Apr W4
File  73:EMBASE 1974-2003/Apr W4
File  34:SciSearch(R) Cited Ref Sci 1990-2003/Apr W4
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
File 144:Pascal 1973-2003/Apr W3
File  99:Wilson Appl. Sci & Tech Abs 1983-2003/Mar
File  65:Inside Conferences 1993-2003/Apr W4
File  94:JICST-EPlus 1985-2003/Apr W3
File  35:Dissertation Abs Online 1861-2003/Mar
File   6:NTIS 1964-2003/Apr W4
Set     Items   Description
S1     612079   'EYE'
S2      81004   'CORNEA'
S3       5035   'SCHLEMM CANAL' OR DC='A9.70.10.790' OR 'SCLERA' OR 'CANAL-
             ,SCHLEMM'
S4        169   'SCHLEMM CANALITIS' OR 'SCHLEMM CANNAL' OR 'SCHLEMM OCCLUS-
            ION' OR 'SCHLEMM S CANAL' OR "SCHLEMM'S CAMAL ENDOTHELIAL CELL
             LINE" OR "SCHLEMM'S CANAL":"SCHLEMM'S CANAL SHORTENING"
S5     204231   'RETINA'
S6     742338   OCUL? OR OPHTHALM? OR INTRAOCULAR OR CORNEA? OR VITREOUS OR
            VITRECTOMY OR VITREORETINAL OR VITRIUM
S7     390497   S TRABECUL? OR RETINA? OR CILIARY
S8     713103   EYE OR EYES OR EYEBALL? OR IRIS OR IRITIS OR SCHLEMM?(2N)CANAL
S9      14156   'HYALURONIDASE'
S10     14156   HYALURONIDASE
S11     63444   'HYALURONOGLUCOSAMINIDASE' OR DC='D4.680.265.10.350' OR R4:R9
S12     93831   'SALINE' OR 'SODIUM CHLORIDE'
S13    102933   'PROTEASE' OR 'PEPTIDE HYDROLASE' OR 'PROTEINASE'
S14      3744   'ENDOPEPTIDASE'
S15    350839   SALINE OR SODIUM()CHLORIDE
S16    218803   PROTEASE OR ENDOPEPTIDASE
S17   4542620   TOPICAL? OR INJECT? OR SURFACE
S18   1291929   S1:S8
S19     74046   S9:S11
S20    350839   S12 OR S15
S21    276272   S13 OR S14 OR S16
S22        32   S18 AND S19(10N)S20
S23     59376   S17(10N)S18
S24        11   S22 AND S23
S25         0   S21 AND S24
S26         5   S24/2002:2003
S27         6   S24 NOT S26
S28         2   RD (unique items)
S29        21   S22 NOT S24
S30        11   RD (unique items)
S31         3   S30/2002:2003
S32         8   S30 NOT S31
S33         8   Sort S32/ALL/PY,D

28/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.
11706777   BIOSIS NO.: 199800488508
Efficacy of hyaluronidase in reducing increases in intraocular pressure
  related to the use of viscoelastic substances.
AUTHOR: Harooni Mark(a); Freilich Jonathan M; Abelson Mark; Refojo Miguel
```

AUTHOR ADDRESS: (a)c/o Miguel Refojo, Schepens Eye Res. Inst., 20 Staniford St., Boston, MA 02114**USA
JOURNAL: Archives of Ophthalmology 116 (9):p1218-1221 Sept., 1998
ISSN: 0003-9950
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: To evaluate the efficacy of hyaluronidase in preventing increases in **intraocular** pressure related to **injections** of hyaluronan-containing viscoelastic substances. Methods: Twenty-five white rabbits were divided into 5 groups. In groups 1 through 4, 0.15 mL of aqueous humor was removed and replaced with 0. 10 mL of a viscoelastic substance in both **eyes** . Additionally, 10 units of hyaluronidase (0.05 mL) was **injected** in the anterior chamber of the right **eye** , whereas the left **eye** was **injected** with a volumetrically equivalent dose of balanced saline solution. Viscoelastic substances tested were Healon and Healon GV (Pharmacia & Upjohn, Kalamazoo, Mich), Viscoat (Alcon Laboratories, Fort Worth, Tex), and Ocucoat (Storz **Ophthalmics** , Clearwater, Fla). In group 5, right **eyes** were **injected** with 10 units of **hyaluronidase** and the left **eyes** were treated with balanced **saline** solution. Results: After **injections** of viscoelastic substance, **intraocular** pressure rose rapidly, reaching a peak at approximately 46 hours after injection and returning to preinjection levels within 24 hours. Hyaluronidase significantly decreased **intraocular** pressure when used with Healon, Healon GV, and Viscoat, but not with Ocucoat. When **injected** in the absence of viscoelastic, hyaluronidase appeared to decrease **intraocular** pressure, but this result was not statistically significant. Conclusions: **Injections** of hyaluronidase into the anterior chamber of rabbits effectively prevent increases in **intraocular** pressure induced by hyaluronan-containing viscoelastic substances. This effect may be related to the ability of hyaluronidase to cleave hyaluronan moieties.

28/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.
07439764 BIOSIS NO.: 000091045753
THE SAFETY OF INTRAVITREAL HYALURONIDASE A CLINICAL AND HISTOLOGIC STUDY
AUTHOR: GOTTLIEB J L; ANTOSZYK A N; HATCHELL D L; SALOUPIS P
AUTHOR ADDRESS: DUKE UNIV. EYE CENT., BOX 3802, DURHAM, NC 27710, USA.
JOURNAL: INVEST OPHTHALMOL VISUAL SCI 31 (11). 1990. 2345-2352. 1990
FULL JOURNAL NAME: Investigative Ophthalmology & Visual Science
CODEN: IOVSD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH
ABSTRACT: The authors previously developed a new model of preretinal neovascularization in the rabbit **eye** using hyaluronidase for enzymatic vitreolysis. The purpose of this study was to evaluate the safety of intravitreal injections of hyaluronidase. Concentrations of 1, 15, 30, 50, and 150 IU of **hyaluronidase** in 0.1 ml of 0.9% **saline** were **injected** intravitreally and aspirated repetitively until the **vitreous** was partially liquified. The animals were examined with indirect **ophthalmoscopy** , fundus photography, and fluorescein angiography before **injection** and on days 1 and 7 after **injection** . Light and electron microscopic **retinal** sections were prepared from enucleated **eyes** at days 1 and 7. All concentrations of hyaluronidase were effective in

duplicate of 15/9/5 on page 12

producing partial vitreolysis. **Eyes** treated with 1 IU showed no abnormalities on days 1 or 7. **Eyes** treated with 15 IU showed no **retinal** abnormalities on day 1, but on day 7 histologic abnormalities were present in two of four **eyes** . At higher concentrations, clinical and histologic changes were seen in proportion to the concentration and included focal whitening, edema, **vitreous** haze, vascular abnormalities, and **retinal** necrosis at the highest doses. Histologic evaluation of the **retina** revealed marked destruction in all layers at the higher concentrations. The authors conclude that 1 IU of intravitreal hyaluronidase is sufficient for partial vitreolysis and nontoxic to the rabbit **retina** .

33/6/4 (Item 4 from file: 73)
05860501 EMBASE No: 1994276974
Glycosaminoglycan and collagen fibrillar interactions in the mouse corneal **stroma**
1994

33/6/5 (Item 5 from file: 34)
02118273 Genuine Article#: KC375 Number of References: 19
Title: ARTERIAL DELIVERY OF MYOBLASTS TO SKELETAL-MUSCLE (Abstract Available)

33/6/6 (Item 6 from file: 5)
03664095 BIOSIS NO.: 000074079672
LOCAL ENVIRONMENTAL FACTORS AND RETINAL **ADHESION IN THE RABBIT**
1982

33/6/7 (Item 7 from file: 5)
01967906 BIOSIS NO.: 000062058019
STROMAL SODIUM BINDING AFTER GLYCOSAMINO GLYCAN DIGESTION
1976

33/6/8 (Item 8 from file: 73)
00832668 EMBASE No: 1977178221
A comparative study of extracellular sulfated glycosaminoglycans synthesized by rabbit corneal **fibroblasts in organ and confluent cultures**
1976

33/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.
13426562 BIOSIS NO.: 200200055383
A dose response study of clonidine with local anesthetic mixture for peribulbar block: A comparison of three doses.
AUTHOR: Madan Rashmi(a); Bharti Neerja; Shende Dilip; Khokhar Sudershan K; Kaul Hira L
AUTHOR ADDRESS: (a)D-II/33, Ansari Nagar, New Delhi, 110029**India E-Mail: rmadan@medinst.ernet.in or rashmimadan@hotmail.com
JOURNAL: Anesthesia & Analgesia 93 (6):p1593-1597 December, 2001
MEDIUM: print
ISSN: 0003-2999
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: Clonidine prolongs anesthesia and analgesia of local anesthetics

in various neural blocks as well as the duration of retrobulbar block. We assessed the dose-response relationship of clonidine added to lidocaine in peribulbar block. Sixty patients undergoing cataract surgery were given peribulbar block with 7 mL of 2% lidocaine and **hyaluronidase** with either **saline** (Control) or clonidine in 0.5-mug/kg (0.5 Clon), 1.0-mug/kg (1.0 Clon), or 1.5-mug/kg (1.5 Clon) doses. The onset and duration of lid and globe akinesia, globe anesthesia and analgesia, postoperative analgesic requirement, and adverse effects (hypotension, bradycardia, hypoxia, sedation, and dizziness) were recorded. The success rate and onset of block were comparable in all groups. The duration of lid and globe akinesia, globe anesthesia and analgesia was significantly ($P<0.01$) prolonged in patients receiving 1.0 and 1.5 mug/kg clonidine as compared with the Control group. Perioperative pain scores and analgesic requirement were significantly less in these groups. 0.5 mug/kg clonidine did not increase the duration of anesthesia and analgesia significantly. Hypotension and dizziness were observed more in patients receiving 1.5 mug/kg clonidine as compared with other groups. We conclude that 1.0 mug/kg clonidine with a mixture of lidocaine (2%) significantly prolonged the duration of anesthesia and analgesia after peribulbar block with limited side effects.

33/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.
12704253 BIOSIS NO.: 200000457755
Alkalinized lidocaine and bupivacaine with hyaluronidase for sub-Tenon's ophthalmic **block.**
AUTHOR: Moharib Magdi M(a); Mitra S
AUTHOR ADDRESS: (a)Department of Anaesthesia/ICU, Sultan Qaboos University Hospital, Muscat, 123**Oman
JOURNAL: Regional Anesthesia and Pain Medicine 25 (5):p514-517 September-October, 2000
MEDIUM: print
ISSN: 1098-7339
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: Background and Objectives: Alkalinization of local anesthetics has been shown to decrease the onset and prolong the duration of block for extraconal and intraconal application in **ocular** surgery. The objective of this study is to determine if alkalinization is also effective in sub-Tenon's block when hyaluronidase is added to the drug mixture. Methods: Twenty-nine patients were randomly assigned to 2 groups in a double-blind, prospective fashion to receive 5.125 mL of either a plain mixture LBH (2.5 mL lidocaine 2%, 2.5 mL bupivacaine 0.5%, 5 IU/mL **hyaluronidase** , and 0.125 mL isotonic **saline**) or pH-adjusted mixture LBH-PH (2.5 mL lidocaine 2%, 2.5 mL bupivacaine 0.5%, 5 IU/mL hyaluronidase, and 0.125 mL sodium bicarbonate 8.4%) of local anesthetics in a 1-quadrant sub-Tenon's block. Time to onset and time to full akinesia were determined every 30 seconds. Results: No difference was found between the study groups. Conclusion: pH adjustment of the local anesthetic mixture of lidocaine, bupivacaine, and hyaluronidase offered no additional benefit in sub-Tenon's technique in **ocular** procedures.

33/7/3 (Item 3 from file: 73)

DIALOG(R)File 73:EMBASE
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07310665 EMBASE No: 1998222658

Peribulbar anaesthesia using a mixture of local anaesthetic and vecuronium

Reah G.; Bodenham A.R.; Braithwaite P.; Esmond J.; Menage M.J.
Dr. A.R. Bodenham, Department of Anaesthesia, The General Infirmary at Leeds, Great George Street, Leeds LS1 3EX United Kingdom

Anaesthesia (ANAESTHESIA) (United Kingdom) 1998, 53/6 (551-554)
CODEN: ANASA ISSN: 0003-2409
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 19

The aim of this double-blind, randomised study was to assess the effects of the addition of 0.5 mg of vecuroniunl bromide to a standard local anaesthetic mixture used for peribulbar anaesthesia. We studied 60 patients undergoing regional anaesthesia for intra- **ocular** surgery and were primarily interested in the quality of globe and lid akinesia. All received a mixture of 5 ml 2% lignocaine with 1:200,000 adrenaline, 5 ml 0.75% bupivacaine and 150 IU **hyaluronidase** with either 0.9% **saline** 0.25 ml (group A, n = 30) or vecuronium bromide 0.25 ml (0.5 mg) (group B, n = 30). **Eye** movements assessed at both 5 and 10 min were significantly reduced in the vecuronium group (group B) ($p < 0.05$). We conclude that the addition of vecuronium at a dose of 0.5 mg to the standard local anaesthetic mixture improves the quality of globe and lid akinesia.

File 149:TGG Health&Wellness DB(SM) 1976-2003/Apr W3
File 636:Gale Group Newsletter DB(TM) 1987-2003/Apr 30
File 441:ESPICOM Pharm&Med DEVICE NEWS 2003/Apr W4
File 442:AMA Journals 1982-2003/Aug B3
File 444:New England Journal of Med. 1985-2003/May W1

Set	Items	Description
S1	125356	EYE OR EYES OR EYEBALL? ?
S2	19056	OCULAR OR CORNEA OR CORNEAL
S3	31869	OPHTHALM? OR INTRAOCULAR OR VITREOUS OR VITRIUM OR VITRECTOMY OR VITREORETINALL
S4	6975	IRIS OR IRITIS OR SCHLEMM?(2N)CANAL
S5	28152	TRABECUL? OR RETINA? OR CILIARY OR RETINO?
S6	506	HYALURONIDASE OR HYALURONOGLUCOSAMINIDASE
S7	17290	SALINE
S8	11692	PROTEASE OR ENDOPEPTIDASE? ?
S9	245252	TOPICAL? OR INJECT? OR SURFACE
S10	156815	S1:S5
S11	6	S6(10N)S7
S12	3	S10(S)S11
S13	**3**	**RD (unique items)**
S14	9	S10 (S)S6(S)S7
S15	6	S14 NOT S12
S16	6	RD (unique items)
S17	0	S16/2002:2003
S18	**6**	**Sort S16/ALL/PD,D**

13/3,AB,K/1 (Item 1 from file: 442)
DIALOG(R)File 442:AMA Journals
(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.
00108300
COPYRIGHT American Medical Association 1998
Efficacy of Hyaluronidase in Reducing Increases in Intraocular Pressure Related to the Use of Viscoelastic Substances (ARTICLE)
HAROONI, MARK; FREILICH, JONATHAN M.; ABELSON, MARK; REFOJO, MIGUEL
Archives of Ophthalmology
Sep, 1998; Laboratory: tzh1218
LINE COUNT: 00273

Objective: To evaluate the efficacy of hyaluronidase in preventing increases in intraocular pressure related to injections of hyaluronan-containing viscoelastic substances. Methods: Twenty-five white rabbits were divided into 5 groups. In groups 1 through 4, 0.15 mL of aqueous humor was removed and replaced with 0.10 mL of a viscoelastic substance in both **eyes** . Additionally, 10 units of hyaluronidase (0.05 mL) was injected in the anterior chamber of the right **eye** , whereas the left **eye** was injected with a volumetrically equivalent dose of balanced saline solution. Viscoelastic substances tested were Healon and Healon GV (Pharmacia & Upjohn, Kalamazoo, Mich), Viscoat (Alcon Laboratories, Fort Worth, Tex), and Ocucoat (Storz **Ophthalmics** , Clearwater, Fla). In group 5, right **eyes** were injected with 10 units of **hyaluronidase** and the left **eyes** were treated with balanced **saline** solution. Results: After injections of viscoelastic substance, intraocular pressure rose rapidly, reaching a peak at approximately 46 hours after injection and returning to preinjection levels within 24 hours. Hyaluronidase significantly decreased intraocular pressure when used with Healon, Healon GV, and Viscoat, but not with Ocucoat. When injected in the absence of viscoelastic, hyaluronidase appeared to decrease intraocular pressure, but this result was not

statistically significant. Conclusions: Injections of hyaluronidase into the anterior chamber of rabbits effectively prevent increases in intraocular pressure induced by hyaluronan-containing viscoelastic substances. This effect may be related to the ability of hyaluronidase to cleave hyaluronan moieties. Arch Ophthalmol. 1998;116:1218-1221

... humor was removed and replaced with 0.10 mL of a viscoelastic substance in both **eyes** . Additionally, 10 units of hyaluronidase (0.05 mL) was injected in the anterior chamber of the right **eye** , whereas the left **eye** was injected with a volumetrically equivalent dose of balanced saline solution. Viscoelastic substances tested were...

... Healon GV (Pharmacia & Upjohn, Kalamazoo, Mich), Viscoat (Alcon Laboratories, Fort Worth, Tex), and Ocucoat (Storz **Ophthalmics** , Clearwater, Fla). In group 5, right **eyes** were injected with 10 units of **hyaluronidase** and the left **eyes** were treated with balanced **saline** solution. Results: After injections of viscoelastic substance, intraocular pressure rose rapidly, reaching a peak at...

...METHODS

The viscoelastic substances and hyaluronidase used in this study are listed in the Table. **Hyaluronidase** for **intraocular** injection was prepared by adding balanced **saline** solution to 150 U of lyophilized bovine testicular **hyaluronidase** (Wydase) to obtain a concentration of 10 U of hyaluronidase in 0.05 mL of...

13/3,AB,K/2 (Item 2 from file: 442)

DIALOG(R)File 442:AMA Journals

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00033467

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Hyaluronidase and Retinal Function (LABORATORY SCIENCES)

WINKLER, BARRY S.

Archives of Ophthalmology

November, 1985; 103: 1743-17461985;

LINE COUNT: 00222 WORD COUNT: 03065

ABSTRACT: Using the incubated isolated rat retina, the effects of hyaluronidase on the electroretinogram (ERG) and metabolic activities were investigated. Initial experiments established the activity of hyaluronidase needed to liquefy, within 15 to 30 minutes, the vitreous of postmortem human eyes; this concentration was 1,000 units/mL. Rat retinas were superfused with a bicarbonate-buffered, oxygenated medium to which hyaluronidase was added in activities ranging from 100 to 5,000 units/mL. These concentrations of hyaluronidase did not significantly alter the amplitudes of the a waves and b waves of the ERG in comparison to their control amplitudes. Measurements were also made of lactic acid production, oxygen consumption, glutathione content, and adenosine triphosphatase activities in control and hyaluronidase-exposed retinas. In the presence of hyaluronidase, their respective values were similar to the controls for all biochemical factors studied. The present experiments demonstrate that addition of hyaluronidase to an "ocular irrigating" solution results in normal ERGs and normal retinal metabolic activity and suggests the possibility that hyaluronidase may be useful in enzyme-assisted vitrectomy. ...hyaluronidase.

In comparison with the excellent preservation of the ERG components when the isolated rat **retina** is bathed in control medium with or without **hyaluronidase** , substitution of a **saline** solution (0.9% NaCl) for the control medium leads to a rapid decline in the...

13/3,AB,K/3 (Item 3 from file: 442)
DIALOG(R)File 442:AMA Journals
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00032339
Copyright (C) 1984 American Medical Association
Shear Flow Characteristics of Sodium Hyaluronate; Relationship to Performance in Anterior Segment Surgery (LABORATORY SCIENCES)
LANG, ELIZABETH; MARK, DAVID; MILLER, FREDERICK A.; MILLER, DAVID; WIK, OVE
Archives of Ophthalmology
July, 1984; 102: 1079-10821984;
LINE COUNT: 00220 WORD COUNT: 03042
ABSTRACT: In this study, methods were developed for the in vitro evaluation of the surgical performance characteristics of viscoelastic fluids, such as sodium hyaluronate (Healon). Sodium hyaluronate exhibited superior surgical performance to chondroitin-6-sulfate. The superior performance of sodium hyaluronate resulted in part from its high viscosity, which is 20 times greater than that of chondroitin-6-sulfate at shear rates on the order of 10 s<-1>. The gel-like character of sodium hyaluronate as evidenced by the creep flow behavior, was greater than that of chondroitin-6-sulfate and was important for maintaining depth in the anterior chamber. It was shown that a threshold of 80 poise for the shear viscosity (at approximately 10 s<-1> was needed for useful performance in surgery. It was also shown that 0.42 USP units of hyaluronidase per 1.0 mg sodium hyaluronate produces a 90% decrease in the shear viscosity (at appoximately 10 s<-1>) within approximately 2 1/2 hours. Use of sodium hyaluronate in conjunction with hyaluronidase would allow sodium hyaluronate to remain highly viscous during surgery, but would gradually become less viscous to facilitate aqueous outflow after surgery. (Arch Ophthalmol 1984; 102: 1079-1082)
... mg/mL and hyaluronidase at a concentration of 150 units/mL were also obtained commercially; **hyaluronidase** was diluted to the desired concentrations with isotonic **saline** solution. All materials were stored at 4 degrees C under sterile conditions until use.
ANTERIOR SEGMENT **EYE** SURGERY
For the anterior segment eye surgery, rabbits were killed by pentobarbitol overdose approximately one...

18/8/1 (Item 1 from file: 149)
DIALOG(R)File 149:(c) 2003 The Gale Group. All rts. reserv.
01931694 SUPPLIER NUMBER: 62892737 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Clinical Trial Methodology to Evaluate Safety and Efficacy of Hyaluronidase in Clearance of Vitreous Hemorrhage.(Abstract)
2000
WORD COUNT: 348 LINE COUNT: 00032
DESCRIPTORS: Diabetes--Research
GEOGRAPHIC CODES/NAMES: 1USA United States

18/8/5 (Item 5 from file: 442)
DIALOG(R)File 442:(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.
00054901
Intraductal Carcinoma of Mammary-Type Apocrine Epithelium Arising Within a Papillary Hydradenoma of the Vulva: Report of a Case and Review of the Literature (Article)
1991;

18/3,AB,K/2 (Item 2 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
(c) 2003 The Gale Group. All rts. reserv.
01724816 SUPPLIER NUMBER: 19903201 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Diagnosis of intraocular lymphoma by flow cytometry.
Davis, Janet L.; Ruiz, Phillip; Viciana, Ana L.
American Journal of Ophthalmology, v124, n3, p362(11)
Sep, 1997
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0002-9394
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 4556 LINE COUNT: 00400
... was already known, demonstrated that excellent results could be obtained, and additional cases were submitted.
Vitrectomy was performed with the balanced **saline** infusion turned on while the surgical assistant manually aspirated 20 to 30 ml of specimen that included disrupted **vitreous** gel and dispersed cells.(8) Other diagnostic tests were performed as indicated. Viral culture or antibody titers were obtained from undiluted **vitreous** aspirated manually from the outflow line of the **vitreous** cutter by the surgical assistant at the beginning of the case. Bacterial and fungal cultures...
...as possible after collection, usually within 20 minutes of collection. Enzymatic digestion of specimen with **hyaluronidase** , as suggested by Wilson and associates,(9) did not improve yield in the one case...

18/3,AB,K/3 (Item 3 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
(c) 2003 The Gale Group. All rts. reserv.
01671958 SUPPLIER NUMBER: 19151300 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Argon laser retinal lesions evaluated in vivo by optical coherence tomography.
Toth, Cynthia A.; Birngruber, Reginald; Boppart, Stephen A.; Hee, Michael R.; Fujimoto, James G.; DiCarlo, Cheryl D.; Swanson, Eric A.; Cain, Clarence P.; Narayan, Drew G.; Noojin, Gary D.; Roach, William P.
American Journal of Ophthalmology, v123, n2, p188(11)
Feb, 1997
PUBLICATION FORMAT: Magazine/Journal ISSN: 0002-9394 LANGUAGE: English
RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 5028 LINE COUNT: 00443
... hydrochloride 0.5%, phenylephrine hydrochloride 2.5%, and tropicamide 1% were administered to the treatment **eye** . Anesthesia was induced with an initial dose of propofol (up to 5 mg/kg) administered...
...5 ml of a 50-50 mixture of lidocaine 2% and bupivacaine 0.75% with **hyaluronidase** was administered to the treatment **eye** to reduce extraocular muscular movement. The cornea was irrigated with sterile **saline** solution as needed to prevent desiccation. At selected time points, immediately before euthanasia and while the animal was under deep anesthesia, the lasertreated **eye** was enucleated. The animals were euthanized while under deep propofol anesthesia, with an overdose of...
...in 3% glutaraldehyde with 0.1 M sodium cacodylate buffer. Within 10 minutes, the posterior **eye** cup was dissected while immersed.
Five eyes of three animals were used for the in...

18/3,AB,K/4 (Item 4 from file: 442)
DIALOG(R)File 442:AMA Journals
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00099458

COPYRIGHT American Medical Association 1996
Maintenance of Replicative Intermediates in Ganciclovir-Treated HumanCytomegalovirus-Infected Retinal Glia (ARTICLE)
BURD, EILEEN M.; PULIDO, JOSE S.; PURO, DONALD G.; O'BRIEN, WILLIAM J.
Archives of Ophthalmology
July, 1996; Laboratory: tzh856
LINE COUNT: 00437

Objectives: To characterize the molecular structure of the human cytomegalovirus (HCMV) DNA maintained in cultures of human retinal glia following ganciclovir treatment and to determine the biological activity of the DNA. Methods: Cultures of human retinal glia were established, infected with HCMV, treated with ganciclovir, and embedded in agarose, and theviral DNA was analyzed by field inversion gel electrophoresis. Results: The HCMV DNA was found to persist in cultures of infected,ganciclovir-treated retinal glial cells in the form of replicative intermediates. After removal of ganciclovir, processed forms of DNA in the 500- to 1000-kilobase range were found as well as 230-kb unit length genome. Infectious virus was recovered after termination of ganciclovir treatment. Conclusion: The data are consistent with the concept that ganciclovir's virostatic nature permits maintenance of HCMV DNA in retinal glia in a biologically active form that is capable of replication after removal of the drug. Arch Ophthalmol. 1996;114:856-861
...in vitro.Antimicrob Agents Chemother. 1983;24:518-521.
MATERIALS AND METHODS
GLIAL CELL CULTURE
Retinal glial cell cultures were established using **retinal** tissue from **eye** bank donor **eyes** ./8/ While no age limit exclusion was set, only **eyes** that were enucleated within 4 to 6 hours of death and reached the laboratory within 24 hours of death were used. **Eyes** that were deemed medically unsuitable by criteria of the **Eye** Bank Association of America were not used. Briefly, the sensory **retinas** were removed from hemisected **eyes** using forceps and scissors. The **retinas** were placed in a solution of calcium- and magnesium-free phosphate buffer with 4% chicken serum, 0.1% trypsin (all reagents from Gibco-BRL, Grand Island, NY), and 0.2% **hyaluronidase** (Sigma, St Louis, Mo) for 45 minutes at 37 degreesC to ... fetal bovine serum, and the cells were dispersed by gentle pipetting. The cells from 2 **retinas** were dispersed into a single 25-cm/2/ tissue culture flask and incubated at 37...
... cells were passaged by treatment with a solution of 0.03% trypsin in phosphate-buffered **saline** containing 0.1-mmol/L ethylenediaminetetraaceti c acid (EDTA) (Sigma) and 3-mmol/L sucrose. As...
... staining for glial fibrillary acidic protein, glutamine synthetase, or with a monoclonalantibody/11/ specific for **retinal** Muller glial cells. Glial cells that were maintained in culture for less than 4 passages...

18/3,AB,K/6 (Item 6 from file: 442)
DIALOG(R)File 442:AMA Journals
(c)2003 Amer Med Assn -FARS/DARS apply. All rts. reserv.
00034523
Copyright (C) 1987 American Medical Association
The Rapid Detection of Acanthamoeba in Paraffin-Embedded Sections of Corneal Tissue With Calcofluor White (CLINICAL SCIENCES)
SILVANY, ROBERT E.; LUCKENBACH, MARTHA W.; MOORE, MARY BETH
Archives of Ophthalmology
October, 1987; 105: 1366-13671987;
LINE COUNT: 00105 WORD COUNT: 01458

ABSTRACT: Acanthamoeba keratitis is a difficult diagnosis to make with routine stains and cultures. Gram's, Giemsa, and hematoxylin-eosin stains do not differentially stain Acanthamoeba, making the detection of organisms difficult. Trophozoite and cyst forms in paraffin-embedded corneal tissue sections can be rapidly and differentially stained with calcofluor white. Under the fluorescence microscope, the trophozoites are bright red-orange, and cyst cell walls fluoresce bright apple-green with red-orange cytoplasm. Retrospective identification can be made by destaining hematoxylin-eosin-stained sections. Digesting background corneal tissue with trypsin or collagenase and hyaluronidase solutions helps to more readily identify trophozoites.
...calcofluor white can be applied as previously described.

To enhance the contrast between Acanthamoeba and **cornea** , the section can be subjected to enzymatic degradation. Deparaffinized **corneal** sections are completely covered directly with 0.25% trypsin in phosphate-buffered **saline** solution or 40 mg of collagenase type 1 and 100 U of **hyaluronidase** type 1-S in 40 mL of Hank's balanced salt solution (Sigma Chemical Co...
... calcofluor white can be applied as previously described. In this procedure, the enzyme will digest **corneal** tissue without affecting the amebic trophozoites or cysts.
RESULTS

Under the fluorescence microscope at X400...

18/7/1 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)
(c) 2003 The Gale Group. All rts. reserv.
01931694 SUPPLIER NUMBER: 62892737 (THIS IS THE FULL TEXT)
Clinical Trial Methodology to Evaluate Safety and Efficacy of Hyaluronidase in Clearance of Vitreous Hemorrhage.(Abstract)
ORELLANA, JUAN; KUPPERMANN, BARUCH D.; THOMAS, EDGAR L.; GIAMPORCARO, JANE ELLEN
Diabetes, 49, 5, A363
May, 2000
TEXT:

Vitrase(R) (**Hyaluronidase**), an investigational drug developed to facilitate clearance of **vitreous** hemorrhage, is currently in Phase III trials to evaluate safety and efficacy for clearance of severe **vitreous** hemorrhage. In order to design the current trials, data were analyzed on rate and frequency of clinically significant hemorrhage clearance through two months following intravitreal injection of this **hyaluronidase** from two previous Phase II multi-centered trials involving 378 subjects, the majority of whom had proliferative diabetic **retinopathy** . Based on the Phase II trial results, inclusion and exclusion criteria for the Phase III trials were established. Primary and secondary endpoints were developed in collaboration with the FDA. Grading scales for **vitreous** hemorrhage density and treatment were developed for both entry criteria and endpoint analysis. Two Phase III multi-centered, prospective, randomized, double-masked trials were established, one for North America and the other primarily European with the addition of sites in Australia, Brazil and South Africa. Based on Phase II data and statistical assumptions, a total of 1190 subjects are to be enrolled in the Phase III trials. Each trial includes evaluation of several dose groups and one **saline** control group. Principal entry criteria are severe **vitreous** hemorrhage defined as red reflex with no view of **retinal** detail posterior to the equator, or no red reflex. Vision at entry must be worse than 20/200 and hemorrhage must be of

at least one month duration. The efficacy endpoint is the frequency of laser to treat underlying cause of the hemorrhage within three months after enrollment. Assessment of safety through one year will include analysis of complications, adverse experiences and visual acuity. The resultant clinical trials are designed to be able to fully assess the safety and efficacy of a non-surgical enzymatic treatment designed to clear **vitreous** hemorrhage.

JUAN ORELLANA,(1)(2) BARUCH D. KUPPERMANN,(1)(2) EDGAR L. THOMAS,(1)(2) JANE ELLEN GIAMPORCARO,(1)(2) STUDY GROUP - VITRASE FOR VITRASE FOR VITREOUS HEMORRHAGE STUDY GROUP, Raleigh, NC; Irvine, CA; Los Angeles, CA

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File 95:TEME-Technology & Management 1989-2003/Apr W2
File 98:General Sci Abs/Full-Text 1984-2003/Mar
File 9:Business & Industry(R) Jul/1994-2003/Apr 30
File 16:Gale Group PROMT(R) 1990-2003/Apr 30
File 160:Gale Group PROMT(R) 1972-1989
File 148:Gale Group Trade & Industry DB 1976-2003/Apr 30
File 621:Gale Group New Prod.Annou.(R) 1985-2003/Apr 30

Set	Items	Description
S1	541398	EYE OR EYES OR EYEBALL? ?
S2	18987	OCULAR OR CORNEA OR CORNEAL
S3	66193	OPHTHALM? OR INTRAOCULAR OR VITREOUS OR VITRIUM OR VITRECTOMY OR VITREORETINALL
S4	24148	IRIS OR IRITIS OR SCHLEMM?(2N)CANAL
S5	29682	TRABECUL? OR RETINA? OR CILIARY OR RETINO?
S6	308	HYALURONIDASE OR HYALURONOGLUCOSAMINIDASE
S7	14087	SALINE
S8	15198	PROTEASE OR ENDOPEPTIDASE? ?
S9	925402	TOPICAL? OR INJECT? OR SURFACE
S10	619499	S1:S5
S11	1	S10(S)S6(S)S7
S12	17	S6 AND S7 AND S10
S13	16	S12 NOT S11
S14	9	RD (unique items)
S15	5	S14/2002:2003
S16	**4**	**S14 NOT S15**

16/7/1 (Item 1 from file: 16)
DIALOG(R)File 16:Gale Group PROMT(R)
(c) 2003 The Gale Group. All rts. reserv.
07917500 Supplier Number: 66198136 (THIS IS THE FULLTEXT)
ISTA Pharmaceuticals Announces Interim Clinical Trial Results.
Business Wire, p0564
Oct 18, 2000
TEXT:
Business Editors/Health and Medical Writers
IRVINE, Calif--(BW HealthWire)--Oct. 18, 2000

ISTA Pharmaceuticals, Inc. (Nasdaq: ISTA), which discovers and develops new remedies for serious diseases and conditions of the **eye** , today announced the interim results of a pilot Phase IIa study showing that Vitrase(R), a drug being developed by the Company, can safely induce a posterior **vitreous** detachment (PVD) in patients with diabetic **retinopathy** . PVD is the separation of the **vitreous** humor (the clear, gel-like substance that fills the back of the **eye**) from the **retina** , and may, according to **retinal** specialists, be beneficial in the early treatment of diabetic **retinopathy** because it delays the progression of the disease. Diabetic **retinopathy** is the leading cause of adult blindness in the United States.

Sixty patients in Mexico City are enrolled in the prospective, randomized, placebo-controlled Phase IIa study. The purpose of the study is to evaluate the safety and efficacy of Vitrase in causing a PVD and its impact on slowing the progression of diabetic **retinopathy** over a one-year period. Patients were randomly assigned to one of four treatment groups and were monitored at regular intervals to determine the degree of PVD. PVD results were documented by ultrasound examinations.

The interim results show that at 16 weeks post-treatment, complete PVDs were documented in 60 percent of **eyes** treated with a single dose of

Vitrase compared with only 6 percent of patients that received a **saline** control. In the other two treatment groups, complete PVDs were documented in 53 percent of **eyes** treated with sulfur-hexafluoride (SF6), a gas that is used as a surgical adjunct in the treatment of **retinal** detachment, and in 50 percent of **eyes** treated with a combination of Vitrase and SF6 gas. In addition, as part of the study, patients will continue to be followed to assess the impact of Vitrase to delay the progression of diabetic **retinopathy** .

The study found that Vitrase safely induced a complete PVD in **eyes** at the non-proliferative, or early stage, of diabetic **retinopathy** . These interim study results will be presented Monday, October 23, 2000, at the annual meeting of the American Academy of **Ophthalmology** in Dallas by one of the study's principal investigators, Federico Graue-Wiechers, M.D., chief of the Department of **Retina** at the Hospital Conde de Valenciana in Mexico City.

Edward H. Danse, ISTA Pharmaceuticals' president and chief executive officer, said the interim study results are encouraging for ISTA. "The results show that Vitrase induced what physicians believe is a beneficial physiological change to the **eye** , which may lead to a potential role for Vitrase in the early treatment of diabetic **retinopathy** , a serious sight-threatening condition that affects approximately 5 million people in the United States," Danse said. "We will continue to evaluate these patients and intend to expand our clinical studies to patients in the United States in the next year as part of our overall plan to study the safety and efficacy of Vitrase in slowing or stopping the progression of diabetic **retinopathy** ."

Diabetic **retinopathy** is a complication of diabetes that impairs eyesight. It is a progressive disease that over time enters a more dangerous, or "proliferative," phase. This phase of the disease is characterized by the growth of abnormal blood vessels on the surface of the **retina** and into the adjoining **vi**treous , which may leak and cause a hemorrhage within the **eye** . There is no cure for diabetic **retinopathy** . Treatment today typically is limited to the use of laser surgery at the proliferative stage of the disease.

ISTA Pharmaceuticals, based in Irvine, Calif., is focused on saving and improving eyesight by developing proprietary products using unique properties of the enzyme **hyaluronidase** . The Company discovers and develops new products that address serious diseases and conditions of the **eye** such as **vitreous** hemorrhage and diabetic **retinopathy** .

Except for historical information contained herein, this press release contains "forward-looking statements," such as statements regarding plans to continue the study of Vitrase for the treatment of diabetic **retinopathy** and the potential benefit of Vitrase for the treatment of diabetic **retinopathy** . These statements are based on current expectations of future events and, as such, involve risks and uncertainties which may cause results to differ materially from those set forth in such statements. These risks and uncertainties include whether or not the Company receives timely and necessary approvals to conduct additional clinical trials for Vitrase for diabetic **retinopathy** and completes clinical trials that demonstrate the safety and efficacy of Vitrase for diabetic **retinopathy** , including the current Phase IIa study and Phase III clinical trials. Further information on the risks and factors that could affect ISTA's business, financial condition, and results of operations are contained in the Company's public disclosure filings with the U.S. Securities and Exchange Commission (SEC), including the Company's Final Prospectus dated August 21, 2000, which are available at www.sec.gov.

Note to Editors: ISTA Pharmaceuticals will be hosting a conference call for analysts and others to discuss third quarter financial results Thursday, October 19, 2000, at 2:00 p.m. (PDT). To participate in the call dial 800-251-7415. A replay will be available from October 19 to October 22 by dialing 800-633-8284, access code 16676916.

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File 350:Derwent WPIX 1963-2003/UD,UM &UP=200326
File 347:JAPIO Oct 1976-2002/Dec(Updated 030402)
File 371:French Patents 1961-2002/BOPI 200209
Set     Items   Description
S1      76195   EYE OR EYES OR EYEBALL? ?
S2      15354   OCULAR OR CORNEA OR CORNEAL
S3      25574   OPHTHALM? OR INTRAOCULAR OR VITREOUS OR VITRIUM OR VITRECT-
             OMY OR VITREORETINALL
S4       6685   IRIS OR IRITIS OR SCHLEMM?(2N)CANAL
S5      11989   TRABECUL? OR RETINA? OR CILIARY OR RETINO?
S6        636   HYALURONIDASE OR HYALURONOGLUCOSAMINIDASE
S7      14454   SALINE
S8      15962   PROTEASE OR ENDOPEPTIDASE? ?
S9    3803746   TOPICAL? OR INJECT? OR SURFACE
S10    112057   S1:S5
S11         3   S10(S)S6(S)S7
S12         6   S6 AND S7 AND S10
S13         3   S12 NOT S11
S14         2   S13 AND S8:S9
S15         1   S13 NOT S14

 11/7/1     (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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013991454
WPI Acc No: 2001-475669/200151
  Use of glycol ether in the manufacture of a medicament for inducing and
  treating retinal detachment
Patent Assignee: ISTA PHARM INC (ISTA-N)
Inventor: KARAGEOZIAN H
Number of Countries: 094  Number of Patents: 002
Patent Family:
Patent No     Kind   Date     Applicat No    Kind   Date     Week
WO 200139765   A2  20010607  WO 2000US42455  A   20001201  200151  B
AU 200145112   A   20010612  AU 200145112    A   20001201  200154
Priority Applications (No Type Date): US 99168830 P 19991203
Patent Details:
Patent No  Kind Lan Pg   Main IPC    Filing Notes
WO 200139765  A2 E  38 A61K-031/00
   Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA
   CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP
   KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT
   RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
   Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR
   IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
AU 200145112  A        A61K-031/00   Based on patent WO 200139765
Abstract (Basic): WO 200139765 A2
      NOVELTY - Use of glycol ether in a medicament to induce retinal
    detachment.
      DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
      (1) a method comprising
      (i) administering a dose of the glycol ether by ocular route to
    induce retinal detachment;
      (ii) translocating a portion of the retinal tissue from a first
    position to a second position; and
      (iii) reattaching the portion of the retinal tissue; and
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(2) protecting the detached retina comprising administering a dose of the glycol ether by ocular route to protect photoreceptor cells in a segment of the detached retina.

ACTIVITY - Ophthalmological.

MECHANISM OF ACTION - None given.

USE - For the induction and treatment of retinal detachment (claimed).

ADVANTAGE - The glycol ether protects photoreceptor cells in a segment of a detached retina and thus protects detached retinal tissue from degeneration. Provides non-surgical retinal translocation. Retinal reattachment is obtained without causing any toxicity. The incidence of cell release into the vitreal space is greatly reduced. The integrity of the retinal tissue following reattachment is substantially less impaired.

pp; 38 DwgNo 0/10

Derwent Class: A96; B05; D16

International Patent Class (Main): A61K-031/00

11/7/2 (Item 2 from file: 350)

DIALOG(R)File 350:Derwent WPIX

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013466292

WPI Acc No: 2000-638235/200061

Delaminating corneal epithelial sheet of human, comprises separating epithelial sheet which is loosened with a solution, and optionally making an incision in the epithelial sheet prior to loosening

Patent Assignee: BOSTON INNOVATIVE OPTICS INC (BOST-N)

Inventor: MILLER D; MILLER D M D

Number of Countries: 020 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200056354	A2	20000928	WO 2000US7253	A	20000317	200061	B
US 6335006	B1	20020101	US 99125387	A	19990322	200207	
			US 2000528459	A	20000317		

Priority Applications (No Type Date): US 99125387 P 19990322; US 2000528459 A 20000317

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200056354	A2	E	21	A61K-038/46	

Designated States (National): JP

Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

US 6335006	B1		A61K-031/47	Provisional application US 99125387

Abstract (Basic): WO 200056354 A2

NOVELTY - Delaminating (D) the epithelial sheet (ES) of the cornea of a human eye having underlying tissue including a stroma which has a top and a middle layer, comprising loosening the ES with a solution including an agent and separating the loosened ES from the underlying tissue of the cornea, is new. An incision is optionally made in the ES prior to the loosening and separating step.

ACTIVITY - Opthalmological.

MECHANISM OF ACTION - None given.

USE - For delaminating or separating the ES of the cornea from the underlying tissue of the cornea (claimed). (D) aids the healing of a defective ES and may be used in conjunction with various form of eye surgery, e.g., refractive eye surgery, without concomitant pain or loss

of vision due to the destruction of the whole or part of the ES.
ADVANTAGE - (D) leaves the ES intact and healthy and may be used in conjunction with various form of eye surgery, e.g., refractive eye surgery, without concomitant pain or loss of vision due to the destruction of the whole or part of the ES.
pp; 21 DwgNo 0/5
Derwent Class: B04; D16
International Patent Class (Main): A61K-031/47; A61K-038/46
International Patent Class (Additional): A61K-038-39; A61K-038-28; A61K-038/46

11/7/3 (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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012773990 **Image available**
WPI Acc No: 1999-580217/199949
Hardening agents for use in correction of refractive errors in the eye
Patent Assignee: ADVANCED CORNEAL SYSTEMS INC (ADCO-N); ISTA PHARM INC (ISTA-N)
Inventor: BAKER P; KARAGEOZIAN H; KARAGEOZIAN V; NESBURN A; PARK J Y
Number of Countries: 085 Number of Patents: 008
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9945869	A1	19990916	WO 99US5135	A	19990309	199949	B
AU 9930739	A	19990927	AU 9930739	A	19990309	200006	
EP 1061873	A1	20001227	EP 99912347	A	19990309	200102	
			WO 99US5135	A	19990309		
CN 1299257	A	20010613	CN 99805898	A	19990309	200158	
KR 2001041806	A	20010525	KR 2000710081	A	20000909	200168	
BR 9908692	A	20011204	BR 998692	A	19990309	200203	
			WO 99US5135	A	19990309		
JP 2002506013	W	20020226	WO 99US5135	A	19990309	200219	
			JP 2000535285	A	19990309		
US 6537545	B1	20030325	US 9877339	P	19980309	200325	
			WO 99US5135	A	19990309		
			US 2000656849	A	20000907		

Priority Applications (No Type Date): US 9877339 P 19980309; US 2000656849 A 20000907
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9945869	A1	E	66	A61F-009/013	
Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
AU 9930739	A				Based on patent WO 9945869
EP 1061873	A1	E		A61F-009/013	Based on patent WO 9945869
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
CN 1299257	A			A61F-009/013	
KR 2001041806	A			A61F-009/013	
BR 9908692	A			A61F-009/013	Based on patent WO 9945869
JP 2002506013	W		91	A61K-045/00	Based on patent WO 9945869
US 6537545	B1			A61K-038/44	Provisional application US 9877339

Cont of application WO 99US5135

Abstract (Basic): WO 9945869 A1

NOVELTY - Correcting refractive errors in the eye comprises administration of a corneal hardening agent, fitting a rigid contact lens to the cornea to reshape it to a desired shape, and removing the lens when reshaping is completed.

DETAILED DESCRIPTION - Correcting refractive errors in the eye of a mammal, comprises:

(a) selecting a corneal hardening agent which causes hardening without corneal damage;

(b) administering the agent;

(c) fitting the cornea with a rigid contact lens with corrective curvature, to reshape the cornea from a first configuration;

(d) allowing the lens to reshape the cornea to a desired second configuration; and

(e) removing the lens when the cornea is able to maintain the desired second configuration unsupported.

USE - The method is used in correcting refractive errors in the eye, as in myopia, hyperopia, and astigmatism; and corneal irregularities, as in keratoconus, contact lens induced corneal intolerance or corneal warpage, corneal ulcers or erosions, corneal melting disorders, pterygium, and irregular corneal shape or uncorrected refractive error caused by corneal surgery. The last includes the prior art corneal techniques of radial or photorefractive keratotomy, laser keratotomileusis in situ (LASIK), or other laser corneal reshaping, thermo- or photothermo- keratoplasty, and corneal transplant or cataract surgery. Optionally, the hardening (and optional softening) agents, together with the rigid corrective lens, can be provided in the form of a kit.

ADVANTAGE - The method allows correction of errors in or on the cornea to an emmetropic (not requiring corrective lenses) shape without surgery. Results are permanent, without tendency for the cornea to go out of shape with time due to softness. The correction can also be achieved in a shorter time, without multiple contact lens changes and follow up examinations lasting many months.

pp; 66 DwgNo 1/5

Derwent Class: A96; B04; B05; D16; P32

International Patent Class (Main): A61F-009/013; A61K-038/44; A61K-045/00

International Patent Class (Additional): A61F-009/00; A61F-009/007; A61K-031/11; A61K-038/46; A61P-027/10

14/7/1 (Item 1 from file: 350)

DIALOG(R)File 350:Derwent WPIX

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014814979 **Image available**

WPI Acc No: 2002-635685/200268

Vaccine for preventing/treating diseases caused by pathogen which infects/avoids destruction by macrophages, has vector having nucleotide sequence encoding pathogen-derived antigen which generates immune response

Patent Assignee: BRACIAK T (BRAC-I); GAULDIE J (GAUL-I); ARKAGEN INC (ARKA-N)

Inventor: BRACIAK T; GAULDIE J

Number of Countries: 096 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week

US 20020086837 A1 20020704 US 2000742892 A 20001221 200268 B
WO 200255104 A2 20020718 WO 2001US49261 A 20011219 200268
Priority Applications (No Type Date): US 2000742892 A 20001221
Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
US 20020086837 A1 12 A61K-048/00
WO 200255104 A2 E A61K-039/02
Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

Abstract (Basic): US 20020086837 A1

NOVELTY - A vaccine (I) useful in preventing and treating diseases caused by a pathogen capable of infecting, or avoiding destruction by, macrophages, comprising a vector which has a nucleotide sequence encoding at least one antigen derived from the pathogen, where the antigen is capable of generating an immune response in its recipient, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a kit comprising a container and one or more patches, having disposed in it a vector comprising a nucleotide sequence encoding an antigen derived from a pathogen capable of infecting, or avoiding destruction by macrophages;

(2) an article of manufacture comprising solution of (I) disposed within a tube, vial, bottle, can or syringe; and

(3) cosmetically improving the appearance of a person's skin who is suffering from acnes vulgaris, by obtaining a composition comprising a mixture of a vector that comprises at least one nucleotide sequence encoding an antigen derived from Propionibacterium acnes, and a cosmetic agent, and administering the composition to the person.

ACTIVITY - Antibacterial; Antiseborrheic; Dermatological; Antiinflammatory; Fungicide; Protozoacide.

No biological data is given.

MECHANISM OF ACTION - Vaccine; Inducer of immune response.

The effect of vaccine containing AdE1 lipase (Ad5E1PBAL) vector on Balb/c female mice (8-14 week) was evaluated. Mice were immunized intramuscularly with 2x10 to the power 9 plaque forming unit (pfu) in 50 micro-l **saline** of AdE1 lipase (Ad5E1PBAL) or control (empty) vector (DL70-3) intramuscularly (I.M.) on left hind leg. 7 days later disease was induced by **injection** of 100 micro-l of 1x10 to the power 9 colony forming unit (cfu)/ml of P. acnes I.M. in phosphate buffered **saline** (PBS) on left rear flank. All recombinant viruses were propagated and purified for the Ad5E1PBAL vector. Control vector DL70-3 was an Ad5 variant deleted in the E1 region. All reactions were measured by caliper sizing. The results demonstrated that pre-immunization with lipase of P. acnes provided protections from P. acnes challenge.

USE - (I) is useful for treating or preventing a disease caused by a pathogen capable of infecting, or avoiding destruction by macrophages, where the pathogen includes Propionibacterium acnes, Listeria monocytogenes, Salmonella typhimurium, Neisseria gonorrhoea, Mycobacterium avium, M. tuberculosis, M. leprae, Brucella abortus, Candida albicans, Leishmania major (claimed). (I) is useful for

eliciting protective immune responses against colonization of the bacterium in skin follicles.

ADVANTAGE - Adenovirus vector in (I) is highly efficient in transferring genetic material to the target cell, has ability to carry large segments of DNA and has the ability to infect non-dividing cells. The gene expression of the vector is transient in the target cell due to lack of integration of the viral DNA into the host cell DNA, which is highly advantageous compared to other vectors which integrate into the chromosomes and cause insertional inactivation or mutation of genes.

DESCRIPTION OF DRAWING(S) - The drawing shows a schematic of the production of a viral vector (Ad5E1PBAL).

pp; 12 DwgNo 1/2

Derwent Class: B04; D16
International Patent Class (Main): A61K-039/02; A61K-048/00
International Patent Class (Additional): A61K-007/48

14/7/2 (Item 2 from file: 350)

DIALOG(R)File 350:Derwent WPIX
(c) 2003 THOMSON DERWENT. All rts. reserv.
012588864 **Image available**
WPI Acc No: 1999-394971/199933
Purification and sequencing of hyaluronidase **isoenzymes**
Patent Assignee: UNIV CALIFORNIA (REGC)
Inventor: CSOKA A; FROST G I; STERN R; WONG T M
Number of Countries: 084 Number of Patents: 005
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9929841	A1	19990617	WO 98US24206	A	19981112	199933	B
AU 9915855	A	19990628	AU 9915855	A	19981112	199946	
EP 1036168	A1	20000920	EP 98960197	A	19981112	200047	
			WO 98US24206	A	19981112		
US 6123938	A	20000926	US 96733360	A	19961017	200051	
			US 97987743	A	19971209		
JP 2001526183	W	20011218	WO 98US24206	A	19981112	200203	
			JP 2000524414	A	19981112		

Priority Applications (No Type Date): US 97987743 A 19971209; US 96733360 A 19961017
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9929841	A1	E	62	C12N-015/11	

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9915855	A		C12N-015/11	Based on patent WO 9929841
EP 1036168	A1	E	C12N-015/11	Based on patent WO 9929841

Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

US 6123938	A		A61K-038/46	CIP of application US 96733360
JP 2001526183	W	68	C07K-014/00	Based on patent WO 9929841

Abstract (Basic): WO 9929841 A1

NOVELTY - A method for purification and sequencing of isoenzymes of plasma **hyaluronidase** (pHAse) found in the urine, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) isolated human urinary **hyaluronidase** (huHAse);

(2) isolated chain A and B polypeptides of huHAse;

(3) polynucleotide sequences encoding the huHAse A or B chain;

(4) a polynucleotide sequence probe comprising at least 15 contiguous nucleotides of the polynucleotide sequence of (3);

(5) a recombinant expression vector comprising polynucleotides encoding huHAse A or B chains;

(6) an isolated recombinant host cell containing the expression vector of (5);

(7) a purified antibody that specifically binds a huHAse or huHAse A or B chain; and

(8) purification of huHAse from a sample comprises contacting the sample with anti-huHAse antibody and detecting for the formation of anti-huHAse antibody-huHAse complexes.

ACTIVITY - Cytostatic; **Ophthalmological** .

MECHANISM OF ACTION - None given.

USE - **Hyaluronidase** is useful as a therapeutic in the treatment of diseases associated with excess hyaluronan and to enhance circulation of physiological fluids and/or therapeutic agents at the site of administration. **Hyaluronidase** can be used to reduce **intraocular** pressure in the **eyes** of glaucoma patients, through degradation of hyaluronan within the **vitreous** humor. It can also be used in cancer therapy as a spreading agent to enhance the activity of chemotherapeutics and/or the accessibility of tumors to chemotherapeutics. In particular, the **hyaluronidase** is useful in cancer therapy for cancers associated with a defect in the tumor suppressor gene LuCa-1 and also in treatment of strokes or myocardial infarction. It can also be used to facilitate clysis, particularly hypodermoclysis and also for treatment of certain lysosomal storage diseases associated with defects in **hyaluronidase** . A lysosomal storage disease amenable to huHAse therapy are those resulting in accumulation of (GlcNAcbeta1-4GlcUAbeta1-3)n (GAGs) due to a defective mannose-6-phosphate pathway.

ADVANTAGE - The purified human urinary **hyaluronidase** is more appropriate for therapeutic uses than the presently available commercial formulations of **hyaluronidase** (e.g. WYDASE, a bovine **hyaluronidase** formulation) which are from a non-human source, which contain two hyaluronidases (rather than one), and which, as determined by SDS-PAGE analysis, are very crude mixtures containing various proteins, including several unidentified proteins and proteins having various biological activities including anticoagulant activities. The current purified huHAse provides a clean source of **hyaluronidase** that is less likely to induce some of the side effects associated with the presently available commercial formulation, and allows better control of the level of activity associated with specific dosages.

Additionally, use of an acid active huHAse is preferred to use of neutral **hyaluronidase** (HAses) since acid active HAses can yield a controlled degradation of a HA substrate and does not degrade all components of the extracellular matrix in the patient. The huHAse also has a lower molecular weight, allowing the enzyme to enter cells more readily than other, higher molecular weight HAses.

DESCRIPTION OF DRAWING(S) - pH activity curve or human urinary **hyaluronidase** using a microtiter assay.

pp; 62 DwgNo 4/4

Derwent Class: B04; D16
International Patent Class (Main): A61K-038/46; C07K-014/00; C12N-015/11
International Patent Class (Additional): A01N-037/18; A61K-038/00; A61K-038/54; A61P-009/10; A61P-027/06; A61P-035/00; C07K-001/00; C07K-016/40; C12N-001/15; C12N-001/19; C12N-001/21; C12N-005/10; C12N-009/42; C12N-015/09; C12Q-001/68; C12R-001-93

15/7/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
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004464246
WPI Acc No: 1985-291124/198547
New crosslinked hyaluronic acid prods. - for medical and cosmetic use, prepd. by reaction with polyfunctional epoxy cpd.
Patent Assignee: SEIKAGAKU KOGYO CO LTD (SEGK)
Inventor: OKUYAMA T; SAKURAI K; UENO Y
Number of Countries: 006 Number of Patents: 015
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
EP 161887	A	19851121	EP 85303183	A	19850503	198547	B
JP 60233101	A	19851119	JP 8488440	A	19840504	198601	
JP 61164558	A	19860725	JP 858512	A	19850122	198636	
JP 61168362	A	19860730	JP 854908	A	19850117	198637	
JP 61172808	A	19860804	JP 8513595	A	19850129	198638	
JP 61210034	A	19860918	JP 8550357	A	19850315	198644	
US 4716224	A	19871229	US 85729558	A	19850502	198802	
US 4863907	A	19890905	US 85748729	A	19850625	198945	
DE 3578961	G	19900906				199037	
EP 161887	B	19910904				199136	
DE 3583963	G	19911010				199142	
JP 93074571	B	19931018	JP 8550357	A	19850315	199345	
JP 94011694	B2	19940216	JP 8513595	A	19850129	199410	
JP 94034814	B2	19940511	JP 858512	A	19850122	199417	
JP 2501551	B2	19960529	JP 8488440	A	19840504	199626	

Priority Applications (No Type Date): JP 8550357 A 19850315; JP 8488440 A 19840504; JP 854908 A 19850117; JP 858512 A 19850122; JP 8513595 A 19850129
Cited Patents: 1.Jnl.Ref; A3...8641; No-SR.Pub
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
EP 161887	A	E	41	P	
Designated States (Regional): FR GB SE					
EP 161887	B			P	
Designated States (Regional): DE FR GB SE					
JP 93074571	B		7	P	Based on patent JP 61210034
JP 94011694	B2		6	P	Based on patent JP 61172808
JP 94034814	B2		4	P	Based on patent JP 61168362
JP 2501551	B2		6	P	Previous Publ. patent JP 60233101
JP 60233101	A			P	
JP 61164558	A			P	
JP 61168362	A			P	
JP 61172808	A			P	
JP 61210034	A			P	
US 4716224	A			P	
US 4863907	A			P	
DE 3578961	G			P	

DE 3583963 G P
Abstract (Basic): EP 161887 A

New crosslinked hyaluronic acids or their salts are prepd. by crosslinking hyaluronic acid (HA), or a HA salt, with a polyfunctional epoxy cpd. (I) to give a prod. with a crosslinking index of at least 5 (pref. at least 10) per 1000 repeating glucuronic acid and N-acetylglucosamine units.

Pref. (I) may be an epihalohydrin or a bisepoxy cpd., e.g. an alpha, omega-(2,3-epoxypropoxy)alkane or a bisphenol diglycidyl ether.

USE - The prods. are useful for treating arthritis or **ophthalmic** disorders (e.g. detached **retina**), as components of skin cosmetics, or for prodn. of medical moulded prods. (e.g. implants). They have better resistance to degradation by **hyaluronidase** than non-crosslinked HA.

Dwg.0/10

Abstract (Equivalent): EP 161887 B

A crosslinked hyaluronic acid or a salt thereof obtainable by crosslinking hyaluronic acid or a salt thereof with a polyfunctional epoxy cpd selected from halomethyloxirane cpds, cpds represented by the following formula (I) wherein n is from 2 to 6, and a diglycidyl ether of bisphenol A or bisphenol F, said crosslinked hyaluronic acid or salt exhibiting water solubility and having a crosslinking index of 5 or more per 1000 repeating disaccharide units composed of glucuronic acid and N-acetylglucosamine. (25pp)

Abstract (Equivalent): US 4863907 A

New high M.W. cross-linked glucosaminoglycan (GAG) or salt is obtd. by crosslinking a glucosaminoglycan (excluding hyaluronic acid) with polyfunctional epoxy cpd. to give cross-linking index of 0.005-1(0.165)/mole repeating dissaccharides. GAG may be chondroitin sulphate, heparan sulphate, heparin, keratin, or keratan sulphate, keratan polysulphate. Epoxy cpd. is epichlorohydrin or epibromohydrin.

New compsn. to apply to **vitreous** body or wound comprises 2% soln. in physiological **saline** with **ophthalmic** carrier, with viscosity below 50000(5000-30000)cp.

USE/ADVANTAGE - To function as natural GAG in development, growth, ageing of tissues and to maintain transparency of **eye** tissues and control water/electrolytes in body fluids without rejection or adverse reaction. Also used for cosmetics and prosthetics (as mouldable complex with collagen), or for use as sustained release drug. Resists enzymes. (18pp)

Derwent Class: A96; B04; D16; D22
International Patent Class (Main): A61K-007/48; A61K-031/725; A61L-027/00
International Patent Class (Additional): A61F-009/00; A61K-007/00; A61K-031/72; C08B-037/08; C08G-059/48

File 348:EUROPEAN PATENTS 1978-2003/Apr W03
File 349:PCT FULLTEXT 1979-2002/UB=20030424,UT=20030417

Set	Items	Description
S1	69445	EYE OR EYES OR EYEBALL? ?
S2	16950	OCULAR OR CORNEA OR CORNEAL
S3	21018	OPHTHALM? OR INTRAOCULAR OR VITREOUS OR VITRIUM OR VITRECTOMY OR VITREORETINALL
S4	8050	IRIS OR IRITIS OR SCHLEMM?(2N)CANAL
S5	25848	TRABECUL? OR RETINA? OR CILIARY OR RETINO?
S6	1820	HYALURONIDASE OR HYALURONOGLUCOSAMINIDASE
S7	75846	SALINE
S8	35440	PROTEASE OR ENDOPEPTIDASE? ?
S9	890823	TOPICAL? OR INJECT? OR SURFACE
S10	102930	S1:S5
S11	9	S10(S)S6(S)S7
S12	**7**	**S11(S)S8:S9**
S13	**2**	**S11 NOT S12**

12/3,K/2 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00884146 **Image available**
PHAKIC OR APHAKIC INTRAOCULAR LENS ASSEMBLY
ENSEMBLE DE LENTILLE INTRA-OCULAIRE POUR OEIL PHAKIQUE OU APHAQUE
Patent Applicant/Inventor:
KELLAN Robert E, 60 East Street, Suite 1100, Methuen, MA 01844, US, US (Residence), US (Nationality)
Legal Representative:
LAPPIN Mark G (et al) (agent), McDermott, Will & Emery, 28 State Street, Boston, MA 02109, US,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200217818 A1 20020307 (WO 0217818)
Application: WO 2001US11473 20010405 (PCT/WO US0111473)
Priority Application: US 2000652505 20000831
Designated States: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 3703
Fulltext Availability:
Claims
Claim
... are preferably lenticular-shaped (shown in Fig. 3) to allow for minimal contact with the **eye** structures yet provide the required stability for the desired visual results. [41] An alternate embodiment...
...with lens assembly 1 0, the lens assembly 20 is an anterior chamber angle supported **intraocular** lens preferably constructed
6
corneal incision. [42] Other non-limiting configurations of haptics are shown in Figures 5A-K. hi...

...A in a manner that interferes with the footplates resting in the angle of the **eye** (see, Fig. 1). [44] The preferred embodiment **intraocular** lens assembly of the invention is designed to be foldable to facilitate insertion through small...

...example, acrylic optics and hydrogel haptics. Where the lens assembly is used in the aphakic **eye** , flexible, but less foldable, materials may be preferred. For example, for the aphakic **eye** , the lens assembly may be made of all !5 PMMA or a composite of PMMA...

...chamber, the posterior chamber sulcus and the posterior chamber bag. [47] Figure 5 shows the **intraocular** lens device 1 0 of the invention implanted in the anterior chamber 32 of the **eye** 30 and fixated in the angle 3 1. Lens assembly 1 0 is positioned in anterior chamber 32, between **cornea** 34 and **iris** 36, with optic body 12 positioned over pupil 38 and haptics 14, with footplates FP...

...into angle 3 1. Movement of natural crystalline lens
7
device 10 does not contact **cornea** 34. [48] With this configuration, the footplates of **intraocular** lens rests in angle 3 1, which steady the **intraocular** lens in the proper position. [49] As mentioned above, the intraocular lens assembly of the invention can be usefully implanted into the **eye** as either a refractive phakic **intraocular** lens assembly or an aphakic **intraocular** lens assembly. Phakic **intraocular** lens implantation is becoming more popular because of their good refractive and visual results and because they are relatively easy to implant in most cases (Zaldivar & Rocha, 36 Int. **Ophthalmol** . Clin. 107-111 (1996); Neuhann et al., 14 J. Refract. Surg. 272-279 (1998); Rosen...

...Cataract Refract. Surg. 607-611 (1998). The implantation can be performed by an ordinarily skilled **ophthalmologist** . Little surgical injury occurs to the **ocular** tissues during such implantation. When the surgical quality is not compromised, the results are highly predictable, immediate, and lasting. , 1
[50] Phakic lens assembly implantation using the **intraocular** lens assembly of the invention has advantages over other forms of surgical vision enhancement. Unlike...

...remains, and the patient doesn't lose the ability to accoininodate. Refractive surgery by phakic **intraocular** lenses among patients with hyperopia is not yet as popular as patients with myopia, but...J. Cataract Refract. Surg. 48-56 (1998)). [51] For a phakic lens assembly implantation, the **intraocular** lens assembly of the invention is preferably located in the anterior chamber of the **eye** . Following the appropriate implantation, the **intraocular** lens of the assembly invention can be either an angle-supported phakic **intraocular** lens located in front of the **iris** (see, Fig. 6) or a sulcus-supported phakic !5 **intraocular** lens located behind the **iris** (contrast with the lens assemblies described in the BACKGROUND OF THE INVENTION). The haptic lens features of the **intraocular** lens assembly of the invention fixate the distal haptic portions of the lens, thus preventing dislocation and slipping or shifting of the **intraocular** lens from its proper position. [52] The implantation assembly of the **intraocular** lens assembly of the invention can ;0 generally be performed as provided by (Singh, emedicine **Ophthalmology** (2000)
http://www.emedicine.com/cgi-bin/foxweb.exe/showsection@d:/el,n/ga?boolc...

...but local anesthesia is preferred. For local anesthesia, 2% lidocaine with 7.5 U/ml **hyaluronidase** can be given 10 minutes before surgery. Orbital compression is applied to make the **eye** soft and to reduce

orbital pressure. [55] For preparation of the surgical field, the periorbital...
...also applied two-three times to the lid margin and the conjunctival fornices. Then, the **eye** is washed with **saline** . [56] An **eye** speculum is used for exposure of the surgical field. Upper and lower lid sutures, as...
...of the speculum. (A sutureless procedure can also be used.) Adhesive plastic, applied to the **surface** of the eyelids, is used to pull the eyelashes. [57] For making small intraoperative incisions, an side port (for example, 0.6 mm) is made in the anterior chamber. This **injection** is started at the opposite limbus. As the aqueous fluid drains, it is replaced, for...
...chamber is not reduced at any time. [58] In one embodiment, for implantation of the **intraocular** lens assembly of the. invention into the **eye** , two side ports are made to introduce the instruments that are used to fix the **iris** to the haptics. The width of the incision depends on the diameter of the **intraocular** lens assembly of the invention (being, for example, 4-5 mm). The incision may be made at the hinbus or in the clear **cornea** . If a pocket section is made, wound closure (see, below) can be made without sutures. The **intraocular** lens assembly of the invention can then be introduced in the precrystalline space with angled-suture forceps the lens is positioned, for example, behind the **iris** on a horizontal axis with a cyclodialysis spatula. The **intraocular** lens assembly of the invention is then manipulated to center the optic on the pupil. During implantation of the phakic **intraocular** lens assembly of the invention into the anterior chamber, the lens is centered and fixed...
...that it does not slip out of position. The lens can be positioned between the **cornea** and the **iris** , but avoiding contact with either to prevent **corneal** damage, proliferation of **corneal** epithelium on the anterior **surface** of the lens causing opacification, or **iritis** . If the lens is not positioned properly with respect to the pupil, too much light may be admitted to the **retina** , causing serious vision
9
difficulties. The haptics generally lodge in the angle of the anterior chamber. Also, the anterior chamber of the **eye** is filled with the aqueous humor, a fluid secreted by the **ciliary** process, passing from the posterior chamber to the anterior chamber through the pupil, and from ...
...implanted lens is positioned so the flow of fluid is not blocked. [591 After the **intraocular** lens assembly of the invention is implanted, the viscoelastic material (if previously introduced into the **eye** chambers) is removed from the anterior and posterior chambers of the **eye** with an aspiration syringe (such as a 24-gauge cannula). The **intraocular** lens assembly of the invention is fixed to the anterior **surface** of the **iris** by the haptics of the lens, To achieve fixation, the haptic holds a fold of the **iris** on either side of the pupil. The anterior chamber is washed thoroughly with **saline** . The pupil is contracted with **intraocular** acetylcholine 1 %, carbachol 0.0 I %, or pilocarpine 0.5% solution. The incision is closed by hydrating the **corneal** incisions. A suture rarely is needed. [60] In another embodiment, for implantation of the **intraocular** lens assembly of the invention, the main incision is made at the ventral area of the **eye** (at the "top" of the **eye** , at " 12 o'clock"). The width is preferably equal to the size of the optic...
...or cannulae, or rely on microhooks to manipulate the optic through a hole in the **surface** of the optic (see discussioti M U.S. Pat.

6,142,999). A vertically-holding...
...holds it steadily. A thin forceps is introduced from the side incision and grasps the **iris** close to the claw, passing a fold of the **iris** through the claw, and results in fixing one of the haptics. Both instruments are withdrawn, and the surgeon changes hands for holding each tool. The anterior chamber of the **eye** is again deepened with viscoelastic material, and the lens-fixation instruments are reintroduced. The second...
...remove all viscoelastic material.
10
WO 02/17818 PCT/USOI/11473
atropine include Isopto Atropine (**eye** drops); Minims Atropine Sulphate (single-dose **eye** drops); Min-I-Jet Atropine (**injection**); Actonorm Powder (combined with antacids and peppermint oil); Atropine-1; Atropine-Care; Atropisol; Isopto Atropine...
...I-Tropine; Isopto Atropine; and Ocu-Tropine. Prior to this invention (i.e., while implanting **intraocular** lenses not having the advantages of the foldable **intraocular** lens assembly of the invention), the patient's **eye** would be atropinized following surgery, to allow for accommodation of the lens of the implanted aphak-ic **intraocular** lens assembly to the **eye** (see discussion, U.S. Pat. 6,051,024). Following surgery, the **ciliary** muscle relaxant (such as atropine) sense.
12
I 1. An **intraocular** lens assembly, comprising:
a lens having a circumferential edge, and a first haptic and a...

12/3,K/4 (Item 4 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00806570 **Image available**
COMPOSITIONS AND METHODS FOR THE INDUCTION AND TREATMENT OF RETINAL DETACHMENTS
COMPOSITIONS ET PROCEDES PERMETTANT D'INDUIRE ET DE TRAITER LES DECOLLEMENTS DE LA RETINE
Patent Applicant/Assignee:
ISTA PHARMACEUTICALS INC, Suite 100, 15279 Alton Parkway, Irvine, CA 92618, US, US (Residence), US (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
KARAGEOZIAN Hampar, 31021 Marbella Vista, San Juan Capistrano, CA 92675, US, US (Residence), US (Nationality), (Designated only for: US)
Legal Representative:
HUNT Dale C (agent), Knobbe, Martens, Olson & Bear, LLP, 16th floor, 620 Newport Center Drive, Newport Beach, CA 92660, US,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200139765 A2-A3 20010607 (WO 0139765)
Application: WO 2000US42455 20001201 (PCT/WO US0042455)
Priority Application: US 99168830 19991203
Designated States: AE AG AL AM AT (utility model) AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ (utility model) DE (utility model) DK (utility model) DM DZ EE (utility model) ES FI (utility model) GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK (utility model) SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 9830
Fulltext Availability:
Detailed Description
Detailed Description
.... hypotory, vitreous opacity, aqueous flare, iris neovascularization and macular pucker.
Example 4
Induction of Reversible **Retinal** Detachment in Rabbits for **Retinal** Translocation usinq
PEG 300 and PEG 400
In this study, 12-pigmented rabbits were divided into 2 groups of 6 animals each. Group I consisted of six animals that were **injected** OD with PEG 300. Each of the animals received were first **injected** intravitreally 50@tl of 75 W. of **hyaluronidase** (ACS). Three days after the administration of **hyaluronidase** , the animals received 501tl of PEG 300. As a control, these same animals received **saline** **injections** OS and thus served as a control group (Group la).
Group 11 consisted of six...
...results of this experiment are summarized in Table 1 0.
The results show that animal **injected** first with 75 W. of **Hyaluronidase** enzyme solution followed 3 days later with a second intravitreal **injection** of PEG 300 or PEG 400 induced **retinal** detachment in the rabbit **eyes** within 48 hours. The detached **retinas** spontaneously re-attached within 3 weeks of the intravitreal **injection** of PEG 300 and PEG 400. The control group that received the sterile **saline** solution did not produce any **retinal** detachments. The intravitreal **injection** of **Hyaluronidase** followed by the intravitreal **injection** of PEG 300 and PEG 400 was determined to be safe by using measurement techniques, like Indirect **Ophthalmoscopy** , Fundus Photography, Light and Electron Microscopy and **Electroretinograpy** .
1 0 Efficacy of inducing retinal detachments and retinal re-attachments were documented by Indirect...
...re-attachment without causing any toxicity.
1 5
-1 7
Table 10
Induction of Reversible **Retinal** Detachment in Rabbits for **Retinal** Translocation usinq PEG 300 and I Rabbit Group 1" Intravitreall 2"
Intravitreal **Retinal** Detachment **Retinal** Reattachment
Number Inaection Inmection at 48 hours at 3 weeks
Post 2" In'ection Post...
...50@d of 75 W. of 50@tl of sterile PEG 300 All All
Treatment **Hyaluronidase** solution -Fundus Photos -Fundus Photos N(
n=6 -P Scans Scans
Group la 30@tl of 75 I.I.I. of 50[tl of sterile **saline** None Not Applicable
Control **Hyaluronidase** solution solution -Fundus Photos -Fundus Photos
n=6 -P Scans Scan
L4 Group 11 50@d of 75 I.U. of 5OVd of sterile PEG 400 All All
Treatment **Hyaluronidase** solution -Fundus Photos -Fundus Photos Nc
n=6 -P Scans Scans
Group Ila 30@d of 75 I.I.I. of 50@tl of sterile **saline** None Not

Applicable
Control **Hyaluronidase** solution solution -Fundus Photos -Fundus Photos n=6 -P Scans -P Scan
Example 5
Induction of Reversible **Retinal** Detachment in Rabbits for **Retinal** Translocation using
Varyinq Concentration of PEG 300
In this study, 8-pigmented rabbits were dividedthese animals were first **injected** intravitreally (OD) with 50@tl of 75 I.I.I. of **Hyaluronidase** solution (Group 1). Fourteen days after the first **injection** these animals received 50 @tl of 1 00% sterile PEG 300 intravitreally. The OS **eye** was used as the untreated control as described in Example 1 (Group la). A second group of two animals, Group 11, was first **injected** intravitreally (OD) with 500 of 75 I.I.I. of 1 0 **Hyaluronidase** solution and then **injected** 14 days later with 50ptl of sterile 75% solution of PEG 300 intravitreally.
The OS...
...The control group does not produce any retinal detachment.
Table 1 1
Induction of Reversible **Retinal** Detachment in Rabbits for **Retinal** Translocation usinQ PE(Rabbit Group 1" Intravitreal 2" Intravitreal **Retinal** Detachment **Retinal** Reattachment
Number Iniection Iniection At 48 hours At 3 weeks Rel
n1
Post 2" Iniection...
...75 I.U. of 50[LI Of Sterile All All No Ai
100% PEG 300 **Hyaluronidase** 100% PEG 300 -Fundus Photos -Fundus Photos were c
Group 11 - OD solution 50@d...
...Scan
Untreated Control
Group [Ila - OS
Untreated
Control
Group lVa -OS
Untreated Control
The intravitreal **injection** of **Hyaluronidase** followed the intravitreal **injection** of PEG 300 was determined to be safe. The efficacy of inducing **retinal** detachment and spontaneous **retinal** re-attachment was demonstrated at PEG 300 concentrations of 100%, 75%, 50% and 25% in **saline** vehicle respectively without causing any toxicity.
Example 6
Retinal Detachment Reversal in Adult Cats Using...

12/3,K/5 (Item 5 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00754217
BIOCHEMICAL METHODS THAT ELIMINATE CORNEAL SCARS, OPACIFICATION AND HAZE
PROCEDES BIOCHIMIQUES PERMETTANT D'ELIMINER LES TAIES, LES OPACIFICATIONS ET LE FLOU DE LA CORNEE
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Patent and Priority Information (Country, Number, Date):
Patent: WO 200066139 A2-A3 20001109 (WO 0066139)
Application: WO 2000US11369 20000428 (PCT/WO US0011369)
Priority Application: US 99131558 19990429
Designated States: AE AG AL AM AT AT (utility model) AU AZ BA BB BG BR BY CA CH CN CR CU CZ CZ (utility model) DE DE (utility model) DK DK (utility model) DM DZ EE EE (utility model) ES FI FI (utility model) GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KR (utility model) KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SK (utility model) SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
(AP) GH GM KE LS MW SD SL SZ TZ UG ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Publication Language: English
Filing Language: English
Fulltext Word Count: 11822
Fulltext Availability:
Detailed Description
Detailed Description
... intermittently exposed to an air:liquid interf ace.
At day 3, test corneas received intrastromal **injections** of **Hyaluronidase** (ACS) reconstituted in sterile **saline** (50011.1120@d) adjacent to the scar, with the bevel of the **injecting** needle pointing towards mid- **cornea** . The control group of corneas were **injected** with **saline** at day 3. All corneas were then returned to culture. The test corneas were subsequently **injected** with **Hyaluronidase** (ACS) (5001U/20gl) on day 7 as described above.
1 0 The corneas were examined...
...3mm in length arcing from Scar resolved
comeal-scleral junction to approx mid- by144 hours
cornea
CB-COt-1 1-1 6 54 M OS 96 HRS Small linear scar 1rnm below mid **cornea**
Scar resolved
by 144 hours
Example IV
Effect of **Hyaluronidase** on the ultrastructure of human donor corneas
Human donor corneas were obtained within 24-48...
...The corneas that were placed in culture were grouped as follows: a) untreated controls; b) **saline** **injected** controls; and c) **Hyaluronidase** **injected** (50011.1/20@tl) treatment group. The corneas were cultured, epithelial side up, in a epithelial **surface** of the tissue was intermittently exposed to an air:liquid interface.
At the end of...
...Two tail
Normal
65/M Tissue N = 20 47.5 0.00 %
48 Hours @
8011' **hyaluronidase** N = 10 56.4 18.62 % 0.00592
48 Hours @
80/M **Saline** 52.7 1 0.97 % 0.56211

LWJ
Results
The results show a 1 8.62 % increase in the reorganization of the collagen fibers 48 hours after the **injection** of **hyaluronidase** enzyme. This magnitude of collagen fiber compaction and reorganization for the 80 year old female **cornea** is very significant statistically from the untreated 65 year old male **cornea** . Intrastromai **injection** of **Hyaluronidase** (ACS) was very effective for effecting **corneal** collagen fiber reorganization.
Example V
Corneal opacity clearing efficacy of Hyaluronidase in humans
In this...

12/3,K/6 (Item 6 from file: 349)
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00514517 **Image available**
USE OF CORNEAL HARDENING AGENTS IN ENZYME ORTHOKERATOLOGY
PROCEDE D'ORTHOKERATOLOGIE ENZYMATIQUE UTILISANT UN AGENT DURCISSEUR DE LA CORNEE
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PARK John Y,
KARAGEOZIAN Vicken,
BAKER Phillip,
NESBURN Anthony,
Inventor(s):
KARAGEOZIAN Hampar,
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KARAGEOZIAN Vicken,
BAKER Phillip,
NESBURN Anthony,
Patent and Priority Information (Country, Number, Date):
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Priority Application: US 9877339 19980309
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Publication Language: English
Fulltext Word Count: 26809
Fulltext Availability:
Detailed Description
Detailed Description
... 20125
Plano 50
SUBSTITUTE SHEET (RULE 26)
Date Treatment Slit Lamp Aided VA Unaided VA **Corneal** Description Biornicroscopy Refraction Refraction I.O.P. Thickness
11/2198 165 Days 0 20/20...
...196 Days 0 20120 20120 0 0.553
Example 9

THE SAFETY AND EFFICACY OF **HYALURONIDASE** AND **TOPICAL** 3%
GLYCERALDEHYDE SOLUTION TREATMENT OF
MILD MYOPIA IN HUMAN PATIENTS
Given the favorable results obtained...and randomly separated into three test groups to test the safety and efficacy of using **hyaluronidase** and a glyceraldehyde solution for treating subjects with sub-optimal visual acuity. Groups one and two received an intrastromal **injection** of **hyaluronidase** (50 and 500 IIJI, respectively), while group three received a control **injection** of **saline** .
Following a two week incubation period after the injection, the three groups were fitted with...

12/3,K/7 (Item 7 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT
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00266221
DEVICE FOR ORBITAL IMPLANT
DISPOSITIF DESTINE A UN IMPLANT ORBITAIRE
Patent Applicant/Assignee:
ORBITAL IMPLANT TECHNOLOGY,
Inventor(s):
PERRY Arthur C,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9414390 A1 19940707
Application: WO 92US11203 19921224 (PCT/WO US9211203)
Priority Application: WO 92US11203 19921224
Designated States: AU BB BG BR CA CS FI HU JP KP KR KZ LK MG MN MW NO PL RO RU SD AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR SN TD TG
Publication Language: English
Fulltext Word Count: 13322
Fulltext Availability:
Claims
Claim
... a photographic representation of an implant showing a peg for direct attachment of an artificial **eye** . FIG* 4 is a photographic representation of an implant showing a ball and socket coupling for direct attachment of an artificial **eye** ,
Example
Surcrical Technigue -- Enucleation
Enucleation is the complete removal of the **eyeball** after severing it from the **eye** muscles and the optic nerve. This example describes the surgical technique of enucleation and replacement...
...general anesthesia, In either case, 4-5 cc of 2% Lido caine with epinephrine and **Hyaluronidase** are given in the retrobulbar space for hemostasis. When a local is being used for...
...with epinephrine may be mixed as a 50@50 mix with 0.75% Bupivacaine and **Hyaluronidase** for a longer duration of effect. A 4-0 silk
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double-armed suture...
...released from the globe. The neurectomy is done using the surgeon's preference, and the **eye** is delivered. As in any enuclea

tion procedure, hemostasis should be well-controlled prior to...its equivalent,
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if sclera is to be used, it is soaked in a **saline** and antibiotic solution (i.e. 30 cc of **saline** with 80 mg of Gentamycin) , A selected PHA implant is soaked in the same solution...
...be entirely removed and
the sclera completely hydrated before soaking it in the antibiotic and **saline** solution. The PHA implant is placed in this scleral shell, and the sclera is sutured...
...eviscerated eyebank globe treated in
alcohol and preserved by treating it in a solution of **saline** and Gentamycin (i.e, 100 cc of **saline** and 40 mg or Gentamycin) and-freezing it, As for using sclera, it is preferred...
...socket unwrapped,
Experience has shown that the movement of the implant and thus the artificial **eye** is greater when the implant is coated or wrapped, The use of other wrapping or...to make an area near the optic nerve the anterior pole. I cut out the **cornea** and placed it into the socket posteriorly, The area where the rectus muscles are to...
...the windows in the sclera for the
35 attachment of the muscles and cutting the **cornea** out and placing it posteriorly, allows more rapid vascularization of the PHA implant. Blood vessels...
...with eviscerations. At the end
of the procedure, 4 cc of 0.75% Bupivacaine are **injected** into the muscle cone for postoperative pain control,
I have used ...decrease the patient's discomfort.
After the dressing is removed, the socket is treated with **topical** antibiotics, and the socket is usually ready for a prosthetic fitting in six weeks.
The...
...then closed over the implant in a normal
fashion.
Since the material has a rough **surface** and has many small spicule-type projections, when not wrapping the material in sclera or...
...I
recommend that a small cap of sclera or fascia be placed between the anterior **surface** of the implant and the Tenon's closure. This gives another barrier of protection and...
...coated or wrapped prior to
insertion in the scleral cavity.
Evisceration, the removal of the **intraocular** contents of the **eye** , can be done with the **cornea** left intact, or
35 with the **cornea** removed. The procedure can be done under a local or general anesthesia. After the appropriate...Tenon' s capsule is done in the quadrants between the
5 rectus muscles. If the **cornea** is to be removed, it is removed at this time and a dissection carried out between the choroid and the sclera to remove the **intraocular** contents, The **intraocular** contents may be saved as a

surgical specimen for examination by pathologists.
If the **cornea** is left intact, an incision in the
sclera approximately 5 to 6 mm, posterior to...
...insertion of the superior rectus
muscle is carried out and extended for 180 degrees, The
intraocular contents are removed with an evisceration
spoon with the dissection being carried out between the...
...of the sclera is scrubbed well to
remove any further residue pigment, Also, if the **cornea**
is left intact,, the epithelium and the endothelium are
removed. The inside of the sclera...
...denature any remaining pigmented cells. The inside of the
sclera is well irrigated with normal **saline** solution,
Hemostasis is maintained with a cautery unit,
Relaxing incisions in the sclera can be...
...the hydroxyapatite implant is placed on the
sterile table and soaked in antibiotic solution and
saline .
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If the implant is not coated,, the hydroxyapatite
implant is then wrapped in...5-0 Vicryl
sutures. Tenon's capsule is then closed over the sclera
and/or **cornea** with interrupted 5-0 Vicryl sutures and then
the conjunctiva is closed with a running...
...SUBSTITUTE SHEET
or (5) in patients who desire to have more motility of the
artificial **eye** , This procedure can be done under local or
eneral anesthesia,
surgical Techniaue
After adequate anesthesia...
...can be placed into this pocket,, wrapped in sclera or unwrapped
and, if the implant **surface** is smooth (such as if it is
pre-coated), no wrapping is necessary. As with...
...implanting the hydroxyapatite implant, in
this or other surgical procedures, it should be soaked in
saline with antibiotic solution,
After placing the implant into the socket, the
anterior soft tissues are...porous hydroxyapatite
(PHA) orbital implant is treated in the same way as any
other an **ophthalmic** patient postoperatively. The socket
is usually ready for a custom-f it prosthesis in six...
...the integrated orbital implant
to be vascularized is variable, See, D,E, Soll, Advances
in **Ophthalmic** , Plastic and Reconstructive Surgery, Vol. 2,
p, 1322, St. Louis, C.V, Mosby Co,, 1987...
...most easily determined by having the ocularist make a
template of the patient's artificial **eye** , In the area of
the pupil , the template has a through-and-through hole,
By placing the template in the socket, the **surface** of the
conjunctiva can be marked through this hole. This
indicates the correct location for drilling.
once the area for drilling has been determined, the
eye is prepped and draped in the usual f ashion. A lid
speculum is placed between replaced in
the hole. The patient's artificial **eye** is replaced over
this peg, and the **eye** is patched for 24 hours. In three

to f our weeks, the patient is sent...
...to have
this peg f it to the posterior surf ace of the artif icial **eye** (FIG. 3), The most common way the implant is coupled to the artif icial **eye** is to have the f lat-headed peg replaced with a peg 13 mm long...
...has a ball on one end,
The ball portion of the peg sits above the **surface** of the conjunctiva. The ocularist then drills a small hemi
35 spherical indentation out of the back of the patient's artificial **eye** , and the ball of the peg fits into this socket, By thi s ball@and-socket coupling, the movement of
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the implant is transferred to the artificial **eye** (FIG, 4)
Alternatively, the flat-headed peg can be attached directly to the posterior **surface** of the artificial **eye** . It cannot be emphasized too strongly that the closure
5 of anterior Tenon's and...
...the PHA implant is not wrapped in sclera or some other material making a smooth **surface** . With the amount of movement that the implant will have by being attached to the...
...not of a concern because it will support f ibrovascular and epithelial growth on its **surface** .
Size of the Orbital Implant:
The purpose of an orbital implant is to prevent retraction of orbital tissues, to replace the volume lost by the removal of the **eye** , to help the prosthesis fit more comfortably and more accurately, and to produce movement of...
...of the orbit will have a major effect on the final appearance of the artificial **eye**.
The volume of the artificial **eye** plus the volume of the orbital implant should be equal to the volume of the **eye** that was removed . If the **eye** is assumed to be a sphere with a diameter of 24 mm, the volume of that sphere is 7,2 cc (v=4 7rR/3) s The average artificial **eye** has a volume of 2.5 cc, Therefore, the volume of the orbital implant should be the difference between the volume of the **eye** removed (7,2 cc) and the volume of the artificial **eye** (2.5 cc). This calculation results in an implant that should supply a volume of...
...volume of various implant sizes
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and the approximate implant sizes to use with **eyes** of different diameters, f
In the past, **ophthalmologists** have been taught that the largest implant that should be used during an enuclea
5...
...consideration. The problem is that the ocularist may not be able to fit an artificial **eye** with enough anterior - posterior thickness to create a realistic anterior chamber depth, Also, there may not be enough thickness to allow the ocularist to later drill the posterior **surface** of the prosthesis to create the socket for the ball-and socket motility peg, When...

...made
thin to prevent a proptotic appearance,, the anterior chamber depth is shallow and the **iris** diaphragm appears to be bowed forward, This gives less than a satisfactory result, This is...
...invention.
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Table 1 - Determination of orbital Implant Size
(A) (B) (C) (D) (E)
EYE SIZE **EYE** PROSTHESIS VOLUME TO IDEAL IMPLANT
VOLUME VOLUME BE REPLACED SIZE
22 mm 5,6 cc...

13/6/1 (Item 1 from file: 349)
00849078
USE OF RETINOID RECEPTOR ANTAGONISTS OR AGONISTS IN THE TREATMENT OF CARTILAGE AND BONE PATHOLOGIES
Publication Year: 2001

13/6/2 (Item 2 from file: 349)
00811916
USE OF RETINOID RECEPTOR ANTAGONISTS IN THE TREATMENT OF CARTILAGE AND BONE PATHOLOGIES
Publication Year: 2001